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To: Sarvamangala Devi **Location:** REM 3C18 **Art Unit:** 1645 Tuesday, June 22, 2004 **Case Serial Number:** 10/088341	**From:** Beverly Shears **Location:** Remsen Bldg. RM 1A54 **Phone:** 571-272-2528 beverly.shears@uspto.gov

Search Notes

125292

Shears, Beverly

From: Devi, Sarvamangala
Sent: Wednesday, June 16, 2004 9:34 AM
To: Shears, Beverly
Subject: 10/088,341

Beverly:

Please perform a text search and an inventors' name search in application 10/088,341.

Claim: A Lactobacillus plantarum expressing a heterologous antigen intracellularly or on the cell surface. [Example: L. plantarum 80 and L. plantarum 256; and a recombinant L. plantarum].

Claim: A Lactobacillus plantarum expressing a heterologous antigen wherein the heterologous antigen is from influenza virus, or a E. coli fimbrial antigen.

Inventors: David Michael Shaw; Robert Jan Leer; and Hendrik Pieter Pouwels.

Thanx.

S. DEVI, Ph.D.
AU 1645
Rems - 3C18

sira Search and Information Resources Administration

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Number of Searches: _____
Number of Databases: 2

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_____ N.A. Sequence
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_____ SDC
_____ DARC/Questel
_____ Other

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Devi, S.
10/088341

FILE 'CAPLUS' ENTERED AT 12:13:30 ON 21 JUN 2004
L1 3339 S (LACTOBACILLUS OR L)(W)PLANTARUM
L2 48 S L1 AND ANTIGEN
L3 13 S L2 AND (INFLUENZA(1A)VIRUS OR COLI)

L3 ANSWER 1 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 07 May 2004
ACCESSION NUMBER: 2004:372049 CAPLUS
DOCUMENT NUMBER: 140:373791
TITLE: Pattern of cytokine responses to gram-positive and gram-negative commensal bacteria is profoundly changed when monocytes differentiate into dendritic cells
AUTHOR(S): Karlsson, Helen; Larsson, Pia; Wold, Agnes E.; Rudin, Anna
CORPORATE SOURCE: Department of Rheumatology and Inflammation Research, Goeteborg University, Goeteborg, Swed.
SOURCE: Infection and Immunity (2004), 72(5), 2671-2678
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The normal gastrointestinal bacterial flora is crucial for the maturation of acquired immunity via effects on **antigen** -presenting cells (APCs). Here the authors investigated how two types of APCs, monocytes and dendritic cells (DCs), react to different bacterial strains typical of the commensal intestinal microflora. Purified human monocytes and monocyte-derived DCs were stimulated with UV-inactivated gram-pos. (**Lactobacillus plantarum** and Bifidobacterium adolescentis) and gram-neg. (Escherichia **coli** and Veillonella parvula) bacterial strains. Monocytes produced higher levels of interleukin 12p70 (IL-12p70) and tumor necrosis factor (TNF), as detected by an ELISA, in response to **L. plantarum** than in response to E. **coli** and V. parvula. In contrast, DCs secreted large amts. of IL-12p70, TNF, IL-6, and IL-10 in response to E. **coli** and V. parvula but were practically unresponsive to **L. plantarum** and B. adolescentis. The lack of a response to the gram-pos. strains correlated with lower surface expression of Toll-like receptor 2 (TLR2) on DCs than on monocytes. The surface expression of TLR4 on DCs was undetectable when it was analyzed by flow cytometry, but blocking this receptor decreased the TNF production in response to V. parvula, indicating that TLR4 is expressed at a low d. on DCs. Gamma interferon increased the expression of TLR4 on DCs and also potentiated the cytokine response to the gram-neg. strains. Thus, when monocytes differentiate into DCs, their ability to respond to different commensal bacteria dramatically changes, and they become unresponsive to probiotic gram-pos. bacteria. These results may have important implications for the abilities of different groups of commensal bacteria to regulate mucosal and systemic immunity.
REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 2 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN

Searcher : Shears 571-272-2528

ED Entered STN: 18 Jan 2004
ACCESSION NUMBER: 2004:41108 CAPLUS
DOCUMENT NUMBER: 140:110105
TITLE: Modified lactic acid bacteria and yeast for delivering nucleic acid and/or protein vaccine to respiratory system to treat infection and cancer
INVENTOR(S): Chen, Wei; Fu, Xiaoli; Nouraini, Sherry; Zhang, Zhiqing
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 30 pp., Cont.-in-part of U.S. Ser. No. 280,769.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2004009937	A1	20040115	US 2003-353137	20030127
US 2004043003	A1	20040304	US 2002-280769	20021025

PRIORITY APPLN. INFO.: US 2002-353885P P 20020131
US 2002-353923P P 20020131
US 2002-353964P P 20020131
US 2002-401465P P 20020805
US 2002-280769 A2 20021025

AB Methods and compostions related to the fields of bacteriol., immunol. and gene therapy are provided. In general modified microflora for the delivery of vaccines, allergens and therapeutics to the mucosal surfaces of the respiratory tract are provided. In particular, the compns. and methods are directed at inducing an M-cell mediated immune response to pathogenic diseases. Specifically, methods of vaccine preparation, delivery and mucosal immunization using a Lactic Acid Bacteria (LAB), yeast and LAB that have been modified through fusion with Escherichia **coli** to either present on its cell surface, or secrete, antigenic epitopes derived from pathogenic microorganisms and/or to secrete a therapeutic protein sequence are disclosed.

L3 ANSWER 3 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 08 Aug 2003
ACCESSION NUMBER: 2003:610197 CAPLUS
DOCUMENT NUMBER: 139:148468
TITLE: Methods and composition for delivering nucleic acids and/or proteins to the respiratory system
INVENTOR(S): Chen, Wei; Fu, Xiaoli; Nouraini, Sherry; Zhang, Zhiqing
PATENT ASSIGNEE(S): Symbigene, Inc., USA
SOURCE: PCT Int. Appl., 78 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003063786	A2	20030807	WO 2003-US2469	20030127
WO 2003063786	A3	20040115		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO

RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2004043003	A1	20040304	US 2002-280769	20021025

PRIORITY APPLN. INFO.:

US 2002-353885P	P	20020131
US 2002-353923P	P	20020131
US 2002-401465P	P	20020805
US 2002-280769	A	20021025
US 2002-353964P	P	20020131

AB Methods and compostions related to the fields of bacteriol., immunol. and gene therapy are provided. In general modified microflora for the delivery of vaccines, allergens and therapeutics to the mucosal surfaces of the respiratory tract are provided. In particular, the compns. and methods are directed at inducing an M-cell mediated immune response to pathogenic diseases. Specifically, methods of vaccine preparation, delivery and mucosal immunization using a Lactic Acid Bacteria (LAB), yeast and LAB that have been modified through fusion with E. **coli** to either present on its cell surface, or secrete, antigenic epitopes derived from pathogenic microorganisms and/or to secrete a therapeutic protein sequence are disclosed.

L3 ANSWER 4 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 08 Aug 2003
ACCESSION NUMBER: 2003:610196 CAPLUS
DOCUMENT NUMBER: 139:148467
TITLE: Methods and composition for delivering nucleic acids and/or proteins to the intestinal mucosa
INVENTOR(S): Chen, Wei; Fu, Xiaoli; Nouraini, Sherry; Zhang, Zhiqing
PATENT ASSIGNEE(S): Symbigene, Inc., USA
SOURCE: PCT Int. Appl., 82 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 4
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003063785	A2	20030807	WO 2003-US2468	20030127
WO 2003063785	A3	20031204		

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ,

NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW,
AM, AZ, BY, KG, KZ, MD, RU, TJ, TM
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT,
LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA,
GN, GQ, GW, ML, MR, NE, SN, TD, TG

PRIORITY APPLN. INFO.: US 2002-353885P P 20020131
US 2002-353923P P 20020131
US 2002-353964P P 20020131
US 2002-401465P P 20020805

AB Methods and compns. are provided for in vivo heterologous nucleic acid delivery using genetically modified microflora. Specifically, compns. and related methods for the delivery of heterologous nucleic acids to the intestinal mucosa of animals are provided. Specifically, generically modified microflora are used to deliver transforming heterologous nucleic acids directly, or genetically modified microflora expressing at least one heterologous nucleic acid are provided. Representative microflora include bacteria, bacterial fusions, and yeast. The heterologous nucleic acid may encode for immunoprotective epitopes (**antigens**) or other gene therapy applications.

L3 ANSWER 5 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 01 Dec 2002
ACCESSION NUMBER: 2002:908174 CAPLUS
DOCUMENT NUMBER: 137:368537
TITLE: Innate immune responses of human neonatal cells to bacteria from the normal gastrointestinal flora
AUTHOR(S): Karlsson, Helen; Hessle, Christina; Rudin, Anna
CORPORATE SOURCE: Department of Rheumatology and Inflammation Research, Goteborg University, Goteborg, 413 46, Swed.
SOURCE: Infection and Immunity (2002), 70(12), 6688-6696
CODEN: INFIBR; ISSN: 0019-9567
PUBLISHER: American Society for Microbiology
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The hygiene hypothesis postulates that the prevalence of allergy has increased due to decreased microbial stimulation early in life, leading to delayed maturation of the immune system. The aim of this study was to examine the cytokine pattern produced from cord blood mononuclear cells relative to adult cells after stimulation with bacterial strains from the normal flora. Mononuclear cells from cord and adult blood samples were stimulated with the following bacteria: Bifidobacterium adolescentis, Enterococcus faecalis, **Lactobacillus plantarum**, Streptococcus mitis, Corynebacterium minutissimum, Clostridium perfringens, Bacteroides vulgatus, Escherichia **coli**, Pseudomonas aeruginosa, Veillonella parvula, and Neisseria sicca. The levels of interleukin 12 (IL-12), tumor necrosis factor alpha (TNF-α), IL-10, and IL-6 were measured by ELISA. The TNF-α production was also analyzed after blocking CD14, Toll-like receptor 2 (TLR-2), and TLR-4 prior to stimulation with bacteria. The levels of IL-12 and TNF-α were similar in cord and adult cells. Gram-pos.

bacteria induced considerably higher levels of IL-12 and TNF-α than gram-neg. bacteria in both cord and adult cells. The levels of IL-6 were significantly higher in newborns than in adults, whereas the levels of IL-10 were similar in newborns and adults. Gram-neg. and gram-pos. bacteria induced similar levels of IL-6 and IL-10 in cord cells. **L. plantarum** bound or signaled through CD14, TLR-2, and TLR-4, whereas E. **coli** acted mainly through CD14 and TLR-4. These results indicate that the innate immune response in newborns to commensal bacteria is strong and also suggest that different bacterial strains may have differential effects on the maturation of the immune system of infants.

REFERENCE COUNT: 44 THERE ARE 44 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 6 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 22 Mar 2001
ACCESSION NUMBER: 2001:207884 CAPLUS
DOCUMENT NUMBER: 134:227335
TITLE: Oral recombinant **Lactobacillus plantarum** vaccines
INVENTOR(S): Shaw, David Michael; Leer, Robert Jan; Pouwels, Peter
PATENT ASSIGNEE(S): Nederlandse Organisatie Voor Toegepast-Natuurwetenschappelijk Onderzoek TNO, Neth.
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1084709	A1	20010321	EP 1999-203056	19990917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2001021200	A1	20010329	WO 2000-GB3575	20000918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1212083	A1	20020612	EP 2000-962689	20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003509469	T2	20030311	JP 2001-524624	20000918
ZA 2002001969	A	20030609	ZA 2002-1969	20020308

PRIORITY APPLN. INFO.: EP 1999-203056 A 19990917

WO 2000-GB3575 W 20000918

AB The present invention relates to an oral vaccine comprising recombinant lactic acid bacteria expressing heterologous **antigen** in vivo intracellularly and/or the surface of the lactic acid bacterium as specific immunogenicity eliciting component for eliciting immunogenicity against the heterologous **antigen**, characterized in that the recombinant lactic acid bacterium is a **Lactobacillus plantarum**. Preferably, the recombinant **Lactobacillus plantarum** comprises an expression vector capable of expressing the heterologous **antigen** intracellularly and/or such that the heterologous **antigen** is exposed on the cell surface under conditions present in the gastrointestinal tract. The recombinant **Lactobacillus plantarum** is preferably a recombinant **Lactobacillus plantarum** 256. The invention also relates to a recombinant **Lactobacillus plantarum**, more specifically a recombinant strain of **Lactobacillus plantarum** 256, for use in the vaccines of the invention; as well as to an expression vector suitable for intracellular expression or exposure of a heterologous **antigen** encoded thereon, said expression vector providing expression in a **Lactobacillus plantarum** of the heterologous **antigen** under conditions existing in the gastrointestinal tract.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 7 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 28 Jul 1999
ACCESSION NUMBER: 1999:460277 CAPLUS
DOCUMENT NUMBER: 131:86865
TITLE: Oral product for the prevention and treatment of infectious gastroenteritides in calves
INVENTOR(S): Mican, Petr; Stepanek, Jan
PATENT ASSIGNEE(S): Medipharm CZ, S.R.O., Czech Rep.
SOURCE: Eur. Pat. Appl., 9 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 930316	A1	19990721	EP 1998-310267	19981215
EP 930316	B1	20040506		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CZ 285883	B6	19991117	CZ 1998-158	19980119
SK 283053	B6	20030204	SK 1998-1718	19981214
AT 266045	E	20040515	AT 1998-310267	19981215

PRIORITY APPLN. INFO.: CZ 1998-158 A 19980119

AB Oral product for the prevention and therapy of infectious gastroenteritis in calves that contents of antibodies to bovine rotavirus, bovine coronavirus and enterotoxigenic strains of

Escherichia **coli** prepared from colostrum of immunized cows and/or egg yolks of immunized hens. It contents also a stabilized live culture of lactacidogenic bacteria. Method of production of antibodies to bovine rotavirus, bovine coronavirus and enterotoxigenic strains of Escherichia **coli** by immunization of cows and/or hens with **antigens** of bovine rotavirus, bovine coronavirus and enterotoxigenic strains of Escherichia **coli**, collection of colostrum from the immunized cows and/or egg yolks from the immunized hens and processing of these semi-products into the administration form, for instance by drying.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 8 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 13 May 1999
ACCESSION NUMBER: 1999:292636 CAPLUS
DOCUMENT NUMBER: 130:308997
TITLE: A Streptococcus pneumoniae homolog of the argF gene of **Lactobacillus plantarum** and development of novel antibiotics
INVENTOR(S): Zalacain, Magdalena; Brown, James Raymond
PATENT ASSIGNEE(S): SmithKline Beecham Corporation, USA
SOURCE: Eur. Pat. Appl., 30 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 913476	A2	19990506	EP 1998-203571	19981022
EP 913476	A3	20000301		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
US 6165763	A	20001226	US 1997-961536	19971030
CA 2248996	AA	19990430	CA 1998-2248996	19981029
JP 11253186	A2	19990921	JP 1998-347733	19981030
US 6706508	B1	20040316	US 1999-432682	19991102

PRIORITY APPLN. INFO.: US 1997-961536 A 19971030

AB The Streptococcus pneumoniae homolog of the cell division gene argF of Escherichia **coli** is identified by sequence homol. The gene and gene product may of use in diagnosis and identification of the pathogen and in screening and development of novel antibiotics (no data).

L3 ANSWER 9 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 06 Feb 1996
ACCESSION NUMBER: 1996:76985 CAPLUS
DOCUMENT NUMBER: 124:143041
TITLE: The potential of Lactobacillus as a carrier for oral immunization: Development and preliminary characterization of vector systems for targeted

delivery of **antigens**
AUTHOR(S): Pouwels, Peter H.; Leer, Rob J.; Boersma, Wim J. A.
CORPORATE SOURCE: TNO Nutrition and Food Research Institute, Molecular Genetics and Gene Technology, P.O. Box 5815, HV Rijswijk, 2280, Neth.
SOURCE: Journal of Biotechnology (1996), 44(1-3), 183-92
CODEN: JBITD4; ISSN: 0168-1656
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Oral administration of lactobacilli evokes mucosal and systemic immune responses against epitopes associated with these organisms (Gerritse et al., 1990, 1991). The adjuvant function of different Lactobacillus species was investigated under the conditions of i.p. injection or oral administration. After i.p. injection of trinitrophenylated chicken γ-globulin, high DTH responses were observed with Lactobacillus casei and **Lactobacillus plantarum**, but low responses with Lactobacillus fermentum and Lactobacillus delbrueckii subsp. bulgaricus. In different exptl. model systems L. casei and **L. plantarum** consistently showed significant adjuvanticity. A series of expression and expression-secretion vectors containing the strong constitutive promoter of the L. casei L-ldh gene or the regulatable promoter of the Lactobacillus amylovorus amy gene (Pouwels and Leer, 1995) was used for the intracellular, extracellular and surface-bound expression of an **influenza virus** antigenic determinant fused to Escherichia **coli** β-glucuronidase. Intracellular expression of the fusion protein amounted to 1-2% of total soluble protein. Lactobacilli synthesizing the fusion protein intracellularly evoked an oral immune response after s.c. priming.

L3 ANSWER 10 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 15 Nov 1991
ACCESSION NUMBER: 1991:602868 CAPLUS
DOCUMENT NUMBER: 115:202868
TITLE: Range of antigenic specificity of bifidobacterial peptidoglycan
AUTHOR(S): Sibiryakova, N. I.; Astaf'ev, D. G.; Mayanskaya, I. V.; Goncharova, G. I.; Lyannaya, A. M.
CORPORATE SOURCE: Nizhegorod. Med. Inst., USSR
SOURCE: Zhurnal Mikrobiologii, Epidemiologii i Immunobiologii (1991), (6), 2-3
CODEN: ZMEIAV; ISSN: 0372-9311
DOCUMENT TYPE: Journal
LANGUAGE: Russian

AB By using IgG isolated from pooled normal human serum, it was found that all bifidobacteria have peptidoglycans of similar antigenic properties. Of 5 taxonomically unrelated spp., the peptidoglycans of Staphylococcus aureus, Staphylococcus epidermidis, and Streptococcus faecalis were more antigenically related to, whereas the peptidoglycans of Escherichia **coli** and **Lactobacillus plantarum** were antigenically diverse from the bifidobacterial peptidoglycans.

L3 ANSWER 11 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 28 Apr 1990
ACCESSION NUMBER: 1990:156557 CAPLUS
DOCUMENT NUMBER: 112:156557
TITLE: Reagents and method for quantitation of bivalent antibody
INVENTOR(S): Kuroka, Shigeru; Sunahara, Noriyuki; Shirai, Akiko; Umibe, Kenzo
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 6 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
JP 01223351	A2	19890906	JP 1988-50847	19880303

PRIORITY APPLN. INFO.: JP 1988-50847 19880303

AB A quant. immunoassay of bivalent antibody is based on the activity measurement of the labeling substance of an **antigen** -antibody complex In-Ag.Ab.Ag-L (In = insol. carrier; Ag = **antigen**; Ab = bivalent antibody; L = label; . = **antigen**-antibody bonding; - = chemical bonding). Particularly, Ab is antibody to tumor necrosis factor (TNF), interleukin, or Escherichia **coli** protein; L is an enzyme; In is fragments of bacteria cell wall; the complex contains at least In-Ag and Ag-L. Thus, anti-TNF antibody in serum was treated with **Lactobacillus plantarum** cell wall fragment-immobilized **antigen** at 37° for 30 min and then with β-galactosidase-labeled **antigen** at 37° for 30 min; the reaction mixture was centrifuged and washed for separation of bound and unbound labeled **antigen**; and the precipitate was treated with buffer containing 2-nitrophenyl-α-D-galactoside, ethylene glycol, and NaN3 for the enzyme activity measurement for anti-TNF antibody determination The detection range was 78-620 μg/mL.

L3 ANSWER 12 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1977:580310 CAPLUS
DOCUMENT NUMBER: 87:180310
TITLE: Insoluble antibodies and their use in enzyme immunoassays or radioimmunoassays
INVENTOR(S): Kurooka, Shigeru; Sunahara, Noriyuki
PATENT ASSIGNEE(S): Dainippon Pharmaceutical Co., Ltd., Japan
SOURCE: Ger. Offen., 57 pp.
CODEN: GWXXBX
DOCUMENT TYPE: Patent
LANGUAGE: German
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE

DE 2713369	A1	19771006	DE 1977-2713369	19770325
DE 2713369	C2	19861204		
JP 52117419	A2	19771001	JP 1976-33333	19760325
JP 61018137	B4	19860510		
JP 53065886	A2	19780612	JP 1976-141879	19761125
JP 60026980	B4	19850626		

PRIORITY APPLN. INFO.: JP 1976-33333 19760325
JP 1976-141879 19761125

AB Insol. antibodies with characteristic IR absorption at .apprx.1040, 1540, and 1640 cm-1 are prepared by chemical binding an antibody to the cell wall of a spherical- or rod-form bacterium or yeast by use of glutardialdehyde following treatment of the cell wall with NaIO4. The bacteria used include: **Lactobacillus plantarum**, Streptococcus faecalis, Micrococcus lysodeikticus, Bacillus subtilis, Escherichia **coli**, Achromobacter aquamarinus, Micrococcus roseus, and Staphylococcus aureus; the yeasts used include Saccharomyces cerevisiae, etc.; and the antibody may be directed against hormones (human chorionic gonadotropin, T3, insulin, thyroxine, testosterone), Igs (G), serum albumin, haptens (diphenylhydantoin, phenobarbital, haloperidol), enzymes, and virus-sp. **antigens**. In addition, an anal. kit for use of the immobilized antibodies for radioimmunoassays or enzyme immunoassays is described.

L3 ANSWER 13 OF 13 CAPLUS COPYRIGHT 2004 ACS on STN
ED Entered STN: 12 May 1984
ACCESSION NUMBER: 1974:503017 CAPLUS
DOCUMENT NUMBER: 81:103017
TITLE: Serologic relation between Hemophilus influenzae, type b, capsular polysaccharide and polyribitol teichoic acids of gram-positive bacteria
AUTHOR(S): Argaman, Meir
CORPORATE SOURCE: Natl. Inst. Child Health Hum. Dev., Natl. Inst. Health, Bethesda, MD, USA
SOURCE: Hemophilus Influenzae, Proc. Conf. (1973), Meeting Date 1972, 49-56. Editor(s): Sell, Sarah H. W. Vanderbilt Univ. Press: Nashville, Tenn.
CODEN: 28GTA5
DOCUMENT TYPE: Conference
LANGUAGE: English

AB The capsular polysaccharide of H. influenzae type b, containing ribose phosphate, cross-reacted serol. with exts. of gram-pos. bacteria that contained polyribitol-phosphate teichoic acids, as well as with the Kf147 **antigen** of some E. **coli** strains, although these 2 cross-reactions differ. While the polysaccharides of S. aureus, H. influenzae type b, and E. **coli** B-139 all shared antigenic determinants, these were not serol. identical. H. influenzae showed at least 2 antigenic determinants. Inhibition studies showed that the monosaccharides had no inhibitory activity, while a phosphate ester of fructose showed inhibitory activity at higher concns. than those inducing maximum inhibition observed for ribitol and ribose phosphate esters.

(FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC,

PHIN, TOXCENTER, PASCAL, DISSABS, FEDRIP' ENTERED AT 12:17:20 ON 21 JUN 2004)
L4 24 S L3
L5 15 DUP REM L4 (9 DUPLICATES REMOVED)

L5 ANSWER 1 OF 15 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2004-098616 [10] WPIDS
CROSS REFERENCE: 2003-636770 [60]; 2003-646091 [61]; 2003-663475 [62]
DOC. NO. NON-CPI: N2004-078672
DOC. NO. CPI: C2004-040696
TITLE: Inducing an immune response in an animal comprises providing an immunogenic composition comprising a microflora organism having an expression vector comprising a heterologous nucleic acid that encodes for an **antigen.**
DERWENT CLASS: B04 C06 D16 P34
INVENTOR(S): CHEN, W; FU, X; NOURAINI, S; ZHANG, Z
PATENT ASSIGNEE(S): (CHEN-I) CHEN W; (FUXX-I) FU X; (NOUR-I) NOURAINI S; (ZHAN-I) ZHANG Z
COUNTRY COUNT: 1
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
US 2004009937	A1	20040115	(200410)*		30

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
US 2004009937	A1	Provisional	US 2002-353885P	20020131
		Provisional	US 2002-353923P	20020131
		Provisional	US 2002-353964P	20020131
		Provisional	US 2002-401465P	20020805
		CIP of	US 2002-280769	20021025
			US 2003-353137	20030127

PRIORITY APPLN. INFO: US 2003-353137 20030127; US 2002-353885P 20020131; US 2002-353923P 20020131; US 2002-353964P 20020131; US 2002-401465P 20020805; US 2002-280769 20021025
AN 2004-098616 [10] WPIDS
CR 2003-636770 [60]; 2003-646091 [61]; 2003-663475 [62]
AB US2004009937 A UPAB: 20040210
NOVELTY - Inducing an immune response in an animal comprises providing an immunogenic composition formulated for intranasal administration to the animal where immunogenic composition comprises a microflora organism having an expression vector comprising a heterologous nucleic acid that encodes for an **antigen.**
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an immunogenic composition comprising an intranasal formulation of a microflora organism having an expression vector that comprises

a heterologous nucleic acid that encodes for an **antigen**.

ACTIVITY - Immunosuppressive; Antibacterial; Virucide. No biological data given.

MECHANISM OF ACTION - Vaccine.

USE - The methods are compositions are useful for inducing an immune response against viral and bacterial infections.

Dwg.0/10

L5 ANSWER 2 OF 15 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER:	2004205076 MEDLINE
DOCUMENT NUMBER:	PubMed ID: 15102775
TITLE:	Pattern of cytokine responses to gram-positive and gram-negative commensal bacteria is profoundly changed when monocytes differentiate into dendritic cells.
AUTHOR:	Karlsson Helen; Larsson Pia; Wold Agnes E; Rudin Anna
CORPORATE SOURCE:	Department of Rheumatology and Inflammation Research, Goteborg University, Goteborg, Sweden.. helen.karlsson@immuno.gu.se
SOURCE:	Infection and immunity, (2004 May) 72 (5) 2671-8. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY:	United States
DOCUMENT TYPE:	Journal; Article; (JOURNAL ARTICLE)
LANGUAGE:	English
FILE SEGMENT:	Priority Journals
ENTRY MONTH:	200406
ENTRY DATE:	Entered STN: 20040423 Last Updated on STN: 20040603 Entered Medline: 20040602

AB The normal gastrointestinal bacterial flora is crucial for the maturation of acquired immunity via effects on **antigen** -presenting cells (APCs). Here we investigated how two types of APCs, monocytes and dendritic cells (DCs), react to different bacterial strains typical of the commensal intestinal microflora. Purified human monocytes and monocyte-derived DCs were stimulated with UV-inactivated gram-positive (**Lactobacillus plantarum** and Bifidobacterium adolescentis) and gram-negative (Escherichia **coli** and Veillonella parvula) bacterial strains. Monocytes produced higher levels of interleukin 12p70 (IL-12p70) and tumor necrosis factor (TNF), as detected by an enzyme-linked immunosorbent assay, in response to **L. plantarum** than in response to E. **coli** and V. parvula. In contrast, DCs secreted large amounts of IL-12p70, TNF, IL-6, and IL-10 in response to E. **coli** and V. parvula but were practically unresponsive to **L. plantarum** and B. adolescentis. The lack of a response to the gram-positive strains correlated with lower surface expression of Toll-like receptor 2 (TLR2) on DCs than on monocytes. The surface expression of TLR4 on DCs was undetectable when it was analyzed by flow cytometry, but blocking this receptor decreased the TNF production in response to V. parvula, indicating that TLR4 is expressed at a low density on DCs. Gamma interferon increased the expression of TLR4 on DCs and also potentiated the cytokine response to the gram-negative strains. Our results indicate that when monocytes differentiate into DCs, their ability to respond to different commensal bacteria dramatically changes, and they become

unresponsive to probiotic gram-positive bacteria. These results may have important implications for the abilities of different groups of commensal bacteria to regulate mucosal and systemic immunity.

L5 ANSWER 3 OF 15 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-646091 [61] WPIDS
CROSS REFERENCE: 2003-636770 [60]; 2003-663475 [62]; 2004-098616 [10]
DOC. NO. CPI: C2003-176802
TITLE: Inducing an immune response in an animal against bacterial or viral infections by providing an immunogenic composition formulated for intranasal administration to the animal.
DERWENT CLASS: B04 D16
INVENTOR(S): CHEN, W; FU, X; NOURAINI, S; ZHANG, Z
PATENT ASSIGNEE(S): (CHEN-I) CHEN W; (FUXX-I) FU X; (NOUR-I) NOURAINI S; (ZHAN-I) ZHANG Z; (SYMB-N) SYMBIGENE INC
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003063786	A2	20030807	(200361)*	EN	78
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
US 2004043003	A1	20040304	(200417)		
AU 2003210688	A1	20030902	(200422)		

APPLICATION DETAILS:

PATENT NO	KIND		APPLICATION	DATE
WO 2003063786	A2		WO 2003-US2469	20030127
US 2004043003	A1	Provisional	US 2002-353885P	20020131
		Provisional	US 2002-353923P	20020131
		Provisional	US 2002-353964P	20020131
		Provisional	US 2002-401465P	20020805
			US 2002-280769	20021025
AU 2003210688	A1		AU 2003-210688	20030127

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 2003210688	A1	Based on	WO 2003063786

PRIORITY APPLN. INFO: US 2002-280769 20021025; US 2002-353885P 20020131; US 2002-353923P 20020131; US 2002-401465P 20020805; US 2002-353964P 20020131

Searcher : Shears 571-272-2528

AN 2003-646091 [61] WPIDS
CR 2003-636770 [60]; 2003-663475 [62]; 2004-098616 [10]
AB WO2003063786 A UPAB: 20040331
NOVELTY - Inducing an immune response in an animal comprising providing an immunogenic composition formulated for intranasal administration to the animal, is new. The immunogenic composition comprises a microflora organism having an expression vector comprising a heterologous nucleic acid that encodes for an **antigen.**

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an immunogenic composition.

ACTIVITY - Virucide; Antibacterial.
No biological data given.
MECHANISM OF ACTION - Vaccine.

USE - The method is useful for inducing an immune response in an animal (claimed) against bacterial or viral infections.
Dwg.0/10

L5 ANSWER 4 OF 15 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2002431931 EMBASE
TITLE: Innate immune responses of human neonatal cells to bacteria from the normal gastrointestinal flora.
AUTHOR: Karlsson H.; Hessle C.; Rudin A.
CORPORATE SOURCE: A. Rudin, Department of Rheumatology, Goteborg University, Guldhedsgatan 10, 413 46 Goteborg, Sweden. anna.rudin@microbio.gu.se
SOURCE: Infection and Immunity, (2002) 70/12 (6688-6696). Refs: 44
ISSN: 0019-9567 CODEN: INFIBR
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English

AB The hygiene hypothesis postulates that the prevalence of allergy has increased due to decreased microbial stimulation early in life, leading to delayed maturation of the immune system. The aim of this study was to examine the cytokine pattern produced from cord blood mononuclear cells relative to adult cells after stimulation with bacterial strains from the normal flora. Mononuclear cells from cord and adult blood samples were stimulated with the following bacteria: Bifidobacterium adolescentis, Enterococcus faecalis, **Lactobacillus plantarum**, Streptococcus mitis, Corynebacterium minutissimum, Clostridium perfringens, Bacteroides vulgatus, Escherichia **coli**, Pseudomonas aeruginosa, Veillonella parvula, and Neisseria sicca. The levels of interleukin 12 (IL-12), tumor necrosis factor alpha (TNF-α), IL-10, and IL-6 were measured by enzyme-linked immunosorbent assay. The TNF-α production was also analyzed after blocking CD14, Toll-like receptor 2 (TLR-2), and TLR-4 prior to stimulation with bacteria. The levels of IL-12 and TNF-α were similar in cord and adult cells. Gram-positive bacteria induced considerably higher levels of IL-12 and TNF-α than gram-negative bacteria in both cord and adult cells. The levels of IL-6 were significantly higher

in newborns than in adults, whereas the levels of IL-10 were similar in newborns and adults. Gram-negative and gram-positive bacteria induced similar levels of IL-6 and IL-10 in cord cells. **L. plantarum** bound or signaled through CD14, TLR-2, and TLR-4, whereas E. **coli** acted mainly through CD14 and TLR-4. These results indicate that the innate immune response in newborns to commensal bacteria is strong and also suggest that different bacterial strains may have differential effects on the maturation of the immune system of infants.

L5 ANSWER 5 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 2002:553032 BIOSIS
DOCUMENT NUMBER: PREV200200553032
TITLE: Lactic acid bacteria inhibit TH2 cytokine production by mononuclear cells from allergic patients.
AUTHOR(S): Pochard, Pierre; Gosset, Philippe; Grangette, Corinne; Andre, Claude; Tonnel, Andre-Bernard; Pestel, Joel [Reprint author]; Mercenier, Annick
CORPORATE SOURCE: INSERM U 416, Institut Pasteur de Lille, 1 Rue du Prof. Calmette, 59019, B. P. 245, Lille, France
SOURCE: Journal of Allergy and Clinical Immunology, (October, 2002) Vol. 110, No. 4, pp. 617-623. print.
CODEN: JACIBY. ISSN: 0091-6749.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 30 Oct 2002
Last Updated on STN: 30 Oct 2002

AB Background: Among factors potentially involved in the increased prevalence of allergic diseases, modification of the intestinal bacteria flora or lack of bacterial stimulation during childhood has been proposed. Lactic acid bacteria (LAB) present in fermented foods or belonging to the natural intestinal microflora were shown to exert beneficial effects on human health. Recent reports have indicated their capacity to reduce allergic symptoms. Objective: The purpose of this investigation was to determine the effect of LAB on the production of type 2 cytokines, which characterize allergic diseases. Methods: PBMCs from patients allergic to house dust mite versus those from healthy donors were stimulated for 48 hours with the related Dermatophagoides pteronyssinus allergen or with a staphylococcal superantigen. The effect of LAB preincubation was assessed by measuring the type 2 cytokine production by means of specific ELISA. Results: The tested gram-positive LAB were shown to inhibit the secretion of TH2 cytokines (IL-4 and IL-5). This effect was dose dependent and was observed irrespective of the LAB strain used. No significant inhibition was induced by the control, gram-negative Escherichia **coli** TG1. Interestingly, LAB reduced the TH2 cytokine production from allergic PBMCs specifically restimulated with the related allergen. The inhibition mechanism was shown to be dependent on **antigen**-presenting cells (ie, monocytes) and on the involvement of IL-12 and IFN-gamma. Conclusion: The tested LAB strains were demonstrated to exhibit an anti-TH2 activity, and thus different strains of this family might be useful in the prevention of allergic diseases.

L5 ANSWER 6 OF 15 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2001-246878 [26] WPIDS
DOC. NO. CPI: C2001-074387
TITLE: Oral vaccine based on recombinant **Lactobacillus plantarum**, useful for protecting against microbial pathogens and allergens, expresses heterologous **antigen**.
DERWENT CLASS: B04 D16
INVENTOR(S): LEER, R J; POUWELS, P; SHAW, D M; POUWELS, P H
PATENT ASSIGNEE(S): (NEDE) NEDERLANDSE ORG TOEGEPAST
COUNTRY COUNT: 95
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
EP 1084709	A1	20010321	(200126)*	EN	19
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
WO 2001021200	A1	20010329	(200126)	EN	
RW: AT BE CH CY DE DK EA ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SL SZ TZ UG ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CR CU CZ DE DK DM DZ EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ PL PT RO RU SD SE SG SI SK SL TJ TM TR TT TZ UA UG US UZ VN YU ZA ZW					
EP 1084709	A9	20010516	(200128)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
AU 2000074337	A	20010424	(200141)		
EP 1212083	A1	20020612	(200239)	EN	
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
JP 2003509469	W	20030311	(200319)		61
CN 1387442	A	20021225	(200324)		
ZA 2002001969	A	20030827	(200362)		67

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
EP 1084709	A1	EP 1999-203056	19990917
WO 2001021200	A1	WO 2000-GB3575	20000918
EP 1084709	A9	EP 1999-203056	19990917
AU 2000074337	A	AU 2000-74337	20000918
EP 1212083	A1	EP 2000-962689	20000918
		WO 2000-GB3575	20000918
JP 2003509469	W	WO 2000-GB3575	20000918
		JP 2001-524624	20000918
CN 1387442	A	CN 2000-815334	20000918
ZA 2002001969	A	ZA 2002-1969	20020308

FILING DETAILS:

PATENT NO	KIND	PATENT NO

Searcher : Shears 571-272-2528

AU 2000074337 A Based on WO 2001021200
EP 1212083 A1 Based on WO 2001021200
JP 2003509469 W Based on WO 2001021200

PRIORITY APPLN. INFO: EP 1999-203056 19990917
AN 2001-246878 [26] WPIDS
AB EP 1084709 A UPAB: 20010515
NOVELTY - An oral vaccine (A) containing a recombinant lactic acid bacterium that expresses a heterologous **antigen** (Ag) in vivo, intracellularly and/or at the cell surface, as the immunogenicity-eliciting component (the bacterium used is **Lactobacillus plantarum**), is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(a) a recombinant **L. plantarum** (strain 256), for use in the vaccines; and

(b) an expression vector for intracellular expression and exposure of Ag by **L. plantarum** under the conditions that exist in the gastrointestinal tract.

ACTIVITY - Virucide; antimicrobial; anti-allergic; fungicide; protozoacide.

MECHANISM OF ACTION - Vaccine; induction of a specific immune response.

L. plantarum containing the plasmid pLP503-TTFC (expressing intracellularly the TTFC tetanus **antigen**) was administered orally (5 multiply 109 cells) to mice. Following two booster doses, the TTFC-specific antibody titer increased to 103 by day 77.

USE - (A) are used to protect against:

(i) a wide range of bacteria, viruses, fungi and protozoa, especially those that colonize the mucosa or gastrointestinal tract; and

(ii) allergens.

ADVANTAGE - The vaccines can be administered safely to all humans, including infants, the elderly and immunocompromised subjects. **L. plantarum** colonizes at least part of the gastrointestinal tract (particularly the small intestines), has good persistence and provides higher-level expression of Ag compared with L. casei. **L. plantarum** is generally recognized as safe and is particularly a food-grade strain.

The recombinant **L. plantarum** persists for over 5, especially 20, days, i.e. longer than **L. plantarum** 80 and preferably longer than strain NCIMB 8826 under the same conditions.

Dwg.0/0

L5 ANSWER 7 OF 15 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 1999271057 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10337020
TITLE: Immunomodulatory effects of **Lactobacillus plantarum** colonizing the intestine of gnotobiotic rats.
AUTHOR: Herias M V; Hessle C; Telemo E; Midtvedt T; Hanson L A; Wold A E
CORPORATE SOURCE: Department of Clinical Immunology, Goteborg

SOURCE: University, Goteborg.. v.herias@immuno.gu.se
Clinical and experimental immunology, (1999 May) 116 (2) 283-90.
Journal code: 0057202. ISSN: 0009-9104.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199906
ENTRY DATE: Entered STN: 19990614
Last Updated on STN: 19990614
Entered Medline: 19990603

AB We have studied the effect of the probiotic strain **Lactobacillus plantarum** 299v on the immune functions of gnotobiotic rats. One group of germ-free rats was colonized with the type 1-fimbriated Escherichia **coli** O6:K13:H1 and another group with the same E. **coli** strain together with **L. plantarum** 299v. One and 5 weeks after colonization, bacterial numbers were determined in the contents of the small intestine, caecum and mesenteric lymph nodes. Small intestinal sections were examined for CD8+, CD4+, CD25+ (IL-2R alpha-chain), IgA+ and MHC class II+ cells and mitogen-induced spleen cell proliferation was determined. Immunoglobulin levels and E. **coli**-specific antibodies were measured in serum. Rats given **L. plantarum** in addition to E. **coli** showed lower counts of E. **coli** in the small intestine and caecum 1 week after colonization compared with the group colonized with E. **coli** alone, but similar levels after 5 weeks. Rats colonized with **L. plantarum** + E. **coli** had significantly higher total serum IgA levels and marginally higher IgM and IgA antibody levels against E. **coli** than those colonized with E. **coli** alone. They also showed a significantly increased density of CD25+ cells in the lamina propria and displayed a decreased proliferative spleen cell response after stimulation with concanavalin A or E. **coli** 1 week after colonization. The results indicate that **L. plantarum** colonization competes with E. **coli** for intestinal colonization and can influence intestinal and systemic immunity.

L5 ANSWER 8 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1999:289413 BIOSIS
DOCUMENT NUMBER: PREV199900289413
TITLE: Human monoclonal IgM DJ binds to ssDNA and human commensal bacteria.
AUTHOR(S): Dimitrijevic, Ljiljana A. [Reprint author]; Radulovic, Marko I.; Ciric, Bogoljub P.; Petricevic, Marijana M.; Inic, Aleksandra B.; Nikolic, Dusanka N.; Apostolski, Slobodan
CORPORATE SOURCE: Immunology Research Center "Branislav Jankovic", Vojvode Stepe 458, 11221 Kumodraz, 11221, Belgrade, Yugoslavia
SOURCE: Human Antibodies, (1999) Vol. 9, No. 1, pp. 37-45. print.
ISSN: 1093-2607.

DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 5 Aug 1999
Last Updated on STN: 5 Aug 1999

AB In this study we tried to elucidate further the crossreactivity pattern and binding characteristics of human monoclonal IgM DJ which is an anti-DNA antibody and possesses Y7 natural idiotope. Isolated IgM DJ and its enzymatically obtained fragments Fab' and (Fab')2 were tested for binding to more than 26 **antigens** and nine bacteria in indirect ELISA. Inhibition of binding studies and examination of the stability of **antigen**-antibody complexes were also done in ELISA assay. IgM DJ bound to single stranded DNA and human lactic acid bacteria, such as L. acidophyllus, B. bifidum and **L. plantarum**. This binding was shown to be mediated through IgM DJ Fab' fragment. High avidity and low affinity of interactions was estimated from the binding curves of Fab', (Fab')2 fragments and whole IgM. The common epitopic motif on both **antigens** were negatively charged phosphodiester moieties. Complexes formed with ssDNA and B. bifidum were resistant to washing with high salt. This suggested that electrostatic attraction was not a strong component of the binding. A novel pattern of natural autoantibody reactivity in a human system related to cross-reactivity with DNA and LAB is described. Possible involvement of LAB in induction of natural anti-DNA antibodies is discussed.

L5 ANSWER 9 OF 15 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1998-558150 [48] WPIDS
DOC. NO. CPI: C1999-175229
TITLE: Piglets peroral treatment agent - based on enterotoxic bacterial strains.
DERWENT CLASS: B04 C03
INVENTOR(S): MICAN, P; STEPANEK, J
PATENT ASSIGNEE(S): (MEDI-N) MEDIPHARM CZ SRO
COUNTRY COUNT: 27
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
CZ 9800859	A3	19981014	(199848)*		
EP 955061	A1	19991110	(199952)B	EN	9
R: AL AT BE CH CY DE DK ES FI FR GB GR IE IT LI LT LU LV MC MK NL PT RO SE SI					
SK 9900237	A3	19991008	(199952)		
CZ 287989	B6	20010314	(200117)		
SK 282945	B6	20030109	(200309)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
CZ 9800859	A3	CZ 1998-859	19980320
EP 955061	A1	EP 1999-301120	19990216
SK 9900237	A3	SK 1999-237	19990224
CZ 287989	B6	CZ 1998-859	19980320
SK 282945	B6	SK 1999-237	19990224

Searcher : Shears 571-272-2528

FILING DETAILS:

PATENT NO	KIND	PATENT NO
CZ 287989	B6 Previous Publ.	CZ 9800859
SK 282945	B6 Previous Publ.	SK 9900237

PRIORITY APPLN. INFO: CZ 1998-859 19980320

AN 1998-558150 [48] WPIDS

AB EP 955061 A UPAB: 19991210 ABEQ treated as Basic
NOVELTY - An oral product (I) for the prevention and therapy of swine gastrointestinal infections is new and comprises at least one specific antibody to porcine rotavirus, porcine coronavirus, enterotoxigenic and enteropathogenic strains of Escherichia **coli**, Clostridium sp., Salmonella sp., Serpulina sp. and protozoan species of Isopora sp. and Cryptosporidium sp., obtained from egg yolks of immunized hens.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the production of (I) comprising separating production of the probiotic component of the product by submersive culture of individual selected lactoacidogenic bacteria Enterococcus faecium, Lactobacillus casei and **Lactobacillus plantarum**.
After the culture is finished, separated from the medium, preserved by freeze drying and it is eventually blended as individual components or in combination with the antibodies of the excipient.
USE - The oral product is useful for the prevention and therapy of infectious diseases of the gastrointestinal tract of swine.
ADVANTAGE - The oral product (I) eliminates the drawbacks of the prior art e.g. rapid denaturation of blood serum antibodies in the gastrointestinal tract and the inability of being able to induce passive local immunity of the gastrointestinal tract.
Dwg.0/0

AB CZ 9800859 A UPAB: 20000531
NOVELTY - An oral product (I) for the prevention and therapy of swine gastrointestinal infections is new and comprises at least one specific antibody to porcine rotavirus, porcine coronavirus, enterotoxigenic and enteropathogenic strains of Escherichia **coli**, Clostridium sp., Salmonella sp., Serpulina sp. and protozoan species of Isopora sp. and Cryptosporidium sp., obtained from egg yolks of immunized hens.
DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for the production of (I) comprising separating production of the probiotic component of the product by submersive culture of individual selected lactoacidogenic bacteria Enterococcus faecium, Lactobacillus casei and **Lactobacillus plantarum**.
After the culture is finished, separated from the medium, preserved by freeze drying and it is eventually blended as individual components or in combination with the antibodies of the excipient.
USE - The oral product is useful for the prevention and therapy of infectious diseases of the gastrointestinal tract of swine.
ADVANTAGE - The oral product (I) eliminates the drawbacks of the prior art e.g. rapid denaturation of blood serum antibodies in the gastrointestinal tract and the inability of being able to induce passive local immunity of the gastrointestinal tract.
Dwg.0/0

L5 ANSWER 10 OF 15 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 97158985 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9006326
TITLE: T cell receptor-alpha beta-deficient mice fail to develop colitis in the absence of a microbial environment.
AUTHOR: Dianda L; Hanby A M; Wright N A; Sebesteny A; Hayday A C; Owen M J
CORPORATE SOURCE: Imperial Cancer Research Fund, London, United Kingdom.
CONTRACT NUMBER: AI27855 (NIAID)
AI38932 (NIAID)
SOURCE: American journal of pathology, (1997 Jan) 150 (1) 91-7.
Journal code: 0370502. ISSN: 0002-9440.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199702
ENTRY DATE: Entered STN: 19970227
Last Updated on STN: 19970227
Entered Medline: 19970207

AB Mice with null mutations in cytokine or T cell receptor (TCR) genes develop intestinal inflammation. In the case of interleukin-2-/- and interleukin-10-/- mice it has been demonstrated that normal intestinal bacterial flora can cause gut pathology. TCR-alpha-/- mice not only develop colitis but also produce a strong antibody response to self-**antigens**, such as double-stranded DNA. It is therefore important to establish whether the intestinal inflammation develops spontaneously or is induced by luminal **antigens**. To address this issue, a germ-free colony of TCR-alpha-/- mice was derived and compared with TCR-alpha-/- mice kept in conventional specific-pathogen-free conditions. Although specific-pathogen-free animals developed colitis with a high level of penetrance, there was no evidence of intestinal pathology in germ-free animals. Furthermore, intestinal inflammation was not seen in TCR-alpha-/- mice colonized with a limited bacterial flora consisting of **Lactobacillus plantarum**, Streptococcus faecalis, S. faecium, and/or Escherichia **coli** . We conclude that intestinal inflammation in TCR-alpha-/- mice does not occur spontaneously nor does it result from the presence of bacteria, per se, but rather it is initiated by a specific organism or group of organisms normally present in the gut flora that have yet to be identified.

L5 ANSWER 11 OF 15 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 1996-442942 [44] WPIDS
DOC. NO. CPI: C1996-139384
TITLE: Use of **Lactobacillus plantarum** having mannose-specific adhesion - to decrease translocation of pathogenic bacteria over intact epithelium, especially bacterial with type 1 fimbriae, e.g. Klebsiella, Proteus and Salmonella.
DERWENT CLASS: B04 D16

INVENTOR(S): ADLERBERTH, I; AHRNE, S; JEPPSSON, B; JOHANSSON, M; MOLIN, G; WOLD, A
PATENT ASSIGNEE(S): (PROB-N) PROBI AB; (PROB-N) PROBE AB
COUNTRY COUNT: 71
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 9629083	A1	19960926	(199644)*	EN	48
RW: AT BE CH DE DK EA ES FI FR GB GR IE IT KE LS LU MC MW NL OA PT SD SE SZ UG					
W: AL AM AT AU AZ BB BG BR BY CA CH CN CZ DE DK EE ES FI GB GE HU IS JP KE KG KP KR KZ LK LR LS LT LU LV MD MG MK MN MW MX NO NZ PL PT RO RU SD SE SG SI SK TJ TM TR TT UA UG US UZ VN					
AU 9651665	A	19961008	(199704)		
NO 9704371	A	19971120	(199806)		
EP 817640	A1	19980114	(199807)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT SE					
BR 9607538	A	19980106	(199810)		
JP 11502703	W	19990309	(199920)		36
AU 702705	B	19990304	(199921)		
KR 98703102	A	19981015	(199950)		
US 6159465	A	20001212	(200067)		
CN 1185111	A	19980617	(200254)		
EP 817640	B1	20030521	(200341)	EN	
R: AT BE CH DE DK ES FI FR GB GR IE IT LI LT LU LV MC NL PT SE					
DE 69628288	E	20030626	(200350)		
ES 2200057	T3	20040301	(200426)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 9629083	A1	WO 1996-SE372	19960325
AU 9651665	A	AU 1996-51665	19960325
NO 9704371	A	WO 1996-SE372	19960325
		NO 1997-4371	19970922
EP 817640	A1	EP 1996-908428	19960325
		WO 1996-SE372	19960325
BR 9607538	A	BR 1996-7538	19960325
		WO 1996-SE372	19960325
JP 11502703	W	JP 1996-528347	19960325
		WO 1996-SE372	19960325
AU 702705	B	AU 1996-51665	19960325
KR 98703102	A	WO 1996-SE372	19960325
		KR 1997-706504	19970919
US 6159465	A	WO 1996-SE372	19960325
		US 1997-913618	19970923
CN 1185111	A	CN 1996-194086	19960325
EP 817640	B1	EP 1996-908428	19960325
		WO 1996-SE372	19960325
DE 69628288	E	DE 1996-628288	19960325
		EP 1996-908428	19960325
		WO 1996-SE372	19960325
ES 2200057	T3	EP 1996-908428	19960325

Searcher : Shears 571-272-2528

FILING DETAILS:

PATENT NO	KIND		PATENT NO
AU 9651665	A	Based on	WO 9629083
EP 817640	A1	Based on	WO 9629083
BR 9607538	A	Based on	WO 9629083
JP 11502703	W	Based on	WO 9629083
AU 702705	B	Previous Publ.	AU 9651665
		Based on	WO 9629083
KR 98703102	A	Based on	WO 9629083
US 6159465	A	Based on	WO 9629083
EP 817640	B1	Based on	WO 9629083
DE 69628288	E	Based on	EP 817640
		Based on	WO 9629083
ES 2200057	T3	Based on	EP 817640

PRIORITY APPLN. INFO: SE 1995-1056 19950323
AN 1996-442942 [44] WPIDS
AB WO 9629083 A UPAB: 19961104
Use of a **Lactobacillus plantarum**, having a mannose-specific adhesion, for the preparation of a pharmaceutical compsn. inhibiting the adherence of pathogenic bacteria expressing mannose-specific adhesions to the epithelial cell surface, is new.

The bacterium is **Lactobacillus plantarum** 299v, deposition number DSM 9843. The **Lactobacillus plantarum** adheres to D-mannose-coated agarose beads.

USE - The adherence brings about an ability to decrease the translocation of pathogenic or potentially pathogenic bacteria over intact intestinal epithelium and therefore reduce their ability to deliver toxic and inflammatory substances to the mucosa, and to decrease the inflammatory damage to the intestine caused by non-specific irritants by creating a microenvironment favourable for the reconstruction of the mucosa. Use of the method may also increase the ability of the bacterium to interact with the immune system and may trigger activation of phagocytes and stimulate the **antigen** preserving cells bringing about enhanced immunity. **Lactobacillus plantarum** can be used to inhibit bacteria expressing type 1 fimbriae, especially a bacterium selected from Klebsiella, Enterobacter, Proteus, Salmonella, Shigella and especially Escherichia **coli**, especially in human vaginal and urethral epithelial cells.
Dwg.0/0

L5 ANSWER 12 OF 15 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 96351470 MEDLINE
DOCUMENT NUMBER: PubMed ID: 8717402
TITLE: The potential of Lactobacillus as a carrier for oral immunization: development and preliminary characterization of vector systems for targeted delivery of **antigens**.
AUTHOR: Pouwels P H; Leer R J; Boersma W J
CORPORATE SOURCE: TNO Nutrition and Food Research Institute, Molecular Genetics and Gene Technology, Rijswijk, Netherlands.
SOURCE: Journal of biotechnology, (1996 Jan 26) 44 (1-3) 183-92.

Searcher : Shears 571-272-2528

Journal code: 8411927. ISSN: 0168-1656.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Biotechnology
ENTRY MONTH: 199610
ENTRY DATE: Entered STN: 19961025
Last Updated on STN: 19961025
Entered Medline: 19961016

AB Oral administration of lactobacilli evokes mucosal and systemic immune responses against epitopes associated with these organisms (Gerritse et al., 1990, 1991). The adjuvant function of different Lactobacillus species was investigated under the conditions of intraperitoneal (i.p.) injection or oral administration. After i.p. injection of trinitrophenylated chicken gamma-globulin, high DTH responses were observed with Lactobacillus casei and **Lactobacillus plantarum**, but low responses with Lactobacillus fermentum and Lactobacillus delbrueckii subsp. bulgaricus. In different experimental model systems L. casei and **L. plantarum** consistently showed significant adjuvanticity. A series of expression and expression-secretion vectors containing the strong constitutive promoter of the L. casei L-ldh gene or the regulatable promoter of the Lactobacillus amylovorus amy gene (Pouwels and Leer, 1995) was used for the intracellular, extracellular and surface-bound expression of an **influenza virus** antigenic determinant fused to Escherichia **coli** beta-glucuronidase. Intracellular expression of the fusion protein amounted to 1-2% of total soluble protein. Lactobacilli synthesizing the fusion protein intracellularly evoked an oral immune response after subcutaneous priming.

L5 ANSWER 13 OF 15 MEDLINE on STN
ACCESSION NUMBER: 91361728 MEDLINE
DOCUMENT NUMBER: PubMed ID: 1716036
TITLE: [The range of antigenic specificity of Bifidobacterium peptidoglycan]. Diapazon antigennoi spetsifichnosti peptidoglikana bifidobakterii.
AUTHOR: Sibiriakova N I; Astaf'ev D G; Maianskaia I V; Goncharova G I; Liannaia A M
SOURCE: Zhurnal mikrobiologii, epidemiologii, i immunobiologii, (1991 Jun) (6) 2-3.
Journal code: 0415217. ISSN: 0372-9311.
PUB. COUNTRY: USSR
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: Russian
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199110
ENTRY DATE: Entered STN: 19911027
Last Updated on STN: 19960129
Entered Medline: 19911009

AB The antigenic relationships of Bifidobacterium bifidum 1 peptidoglycans with different strains of this species (LVA-3, 791, GO-4), bifidobacteria of other species (B. adolescentis GO-13, B. breve 79-38, B. lactentis 79-41, B. longum GO-3) and bacteria of

remote taxonomic groups (Streptococcus faecalis 6-3. Staphylococcus aureus COM 885, S. epidermidis COM 2124. **Lactobacillus plantarum** 1, Escherichia **coli** M-17) were studied on the basis of a highly sensitive test system permitting the registration of normal human antibodies to peptidoglycans. The level of cross reactions with staphylococci and streptococci correspond to intraspecific and antigenic affinity to **L. plantarum** and E. **coli** was considerably less pronounced. Copying a number of epitopes of bifidobacteria, S. aureus peptidoglycan seems to possess additional antigenic determinants which participate in the formation of immunological responsiveness in man.

L5 ANSWER 14 OF 15 DISSABS COPYRIGHT (C) 2004 ProQuest Information and Learning Company; All Rights Reserved on STN

ACCESSION NUMBER: 87:2813 DISSABS Order Number: AARC045580 (not available for sale by UMI)
TITLE: MICROBIOLOGICAL ASPECTS OF OESOPHAGOGASTRIC LESIONS IN PIGS
AUTHOR: EMBAYE, HAILU [PH.D.]
CORPORATE SOURCE: UNIVERSITY OF LIVERPOOL (UNITED KINGDOM) (0722)
SOURCE: Dissertation Abstracts International, (1987) Vol. 49, No. 4C, p. 556. Order No.: AARC045580 (not available for sale by UMI). 430 pages. UNIVERSITY'S LIBRARY, UNIVERSITY OF LIVERPOOL, LIVERPOOL, ENGLAND.
DOCUMENT TYPE: Dissertation
FILE SEGMENT: DAI
LANGUAGE: English
ENTRY DATE: Entered STN: 19921118
Last Updated on STN: 19921118

AB Factors related to husbandry and diet influencing the development of parakeratototic lesions and ulcers in the oesophagogastric region of the porcine stomach and the microbiological changes in the region have been investigated under experimental condition and in field material.

Parakeratotic lesions were less prevalent when a coarse diet with a modulus of fineness of grinding (m.f.g.) of more than 2.46 was used than with a fine diet (m.f.g 1.50). More severe parakeratotic lesions and ulcers developed only when the fine diet was used and lesions occurred in pigs as early as 10 weeks of age.

Lactobacilli were the most dominant organisms of the pars oesophagea region. However, streptococci, Escherichia **coli** and yeasts were also detected and isolated in relatively large numbers. Of the Lactobacillus spp., L. fermentum followed by L. salivarius and L. acidophilus were the most frequent. Other species isolated were **L. plantarum**, L. casei, L. brevis, L. confusus, L. viridescens and L. delbrueckii. Biochemically, two distinctive fermentation patterns of L. fermentum strains were established, some fermenting D-fructose and mannose and others failing to ferment both substrates. Serologically, a wide range of cross-reactions occurred between the different spp. of lactobacilli and individual species showed antigenic heterogenicity. However, it was possible to obtain 76.3% correlation between the serological and biochemical results.

Lactobacilli were fewer in number in stomach lesions than in normal epithelium, but erosion rather than parakeratosis influenced

their number. Adhesion studies revealed that only strains of L. fermentum, L. salivarius and L. acidophilus adhered to isolated squamous epithelial cells of the distal oesophagus. Of the streptococci, Str. faecalis and Str. suis type 2 possessing the D and R **antigens** adhered to the squamous epithelial cells. On the other hand, the number of yeasts increased significantly with the age of the pigs and with the severity of the lesions. Invasion by yeast cells and pseudomycelial forms of Candida was more frequent in field material than in experimental pigs and yeasts were isolated mostly from stomachs with parakeratotic lesions. C. albicans and C. glabrata were the species frequently associated with the stomach lesions.

L5 ANSWER 15 OF 15 BIOSIS COPYRIGHT 2004 BIOLOGICAL ABSTRACTS INC. on STN

ACCESSION NUMBER: 1977:133970 BIOSIS
DOCUMENT NUMBER: PREV197763028834; BA63:28834
TITLE: SELECTIVE ADSORPTION OF HETEROPHILE POLY GLYCERO PHOSPHATE **ANTIGEN** FROM **ANTIGEN** EXTRACTS OF STREPTOCOCCUS-MUTANS AND OTHER GRAM POSITIVE BACTERIA.
AUTHOR(S): HAMADA S; TAI S; SLADE H D
SOURCE: Infection and Immunity, (1976) Vol. 14, No. 4, pp. 903-910.
CODEN: INFIBR. ISSN: 0019-9567.
DOCUMENT TYPE: Article
FILE SEGMENT: BA
LANGUAGE: Unavailable

AB Hot saline extracts of S. mutans contain antigenic substances which occasionally react nonspecifically with some antisera against whole cells of various serological groups and types of streptococci. Chromatography of the extract of S. mutans strain MT703 (serotype e) on a DEAE-Sephadex A-25 column gave 2 principal **antigens**. One **antigen** was eluted without adsorption to the resin and was identified as the serotype-specific polysaccharide. The other **antigen**, which contained a large quantity of P, was adsorbed to and released from the resin by gradient elution. It was reactive against the antisera specific for polyglycerophosphate (PGP) from group A S. pyogenes and/or S. mutans strain Ingbritt (type c). The PGP **antigen** was further purified by gel filtration with Sephadex G-75. Two peaks, PGP-1 and PGP-2, were obtained. Each possessed the same antigenic specificity to anti-PGP serum as shown by immunodiffusion. Chemical analyses revealed that the molar ratio of P to glycerol in both was about 1:1, although the protein content between the 2 was significantly different. PGP **antigen** was found to be widely distributed in hot saline extracts from various gram positive bacteria [Streptococcus spp. of Groups A,C,D,E,H,G,L,N and R, S. sanguis, S. salivarius, S. bovis, S. mitis, **Lactobacillus plantarum**, L. casei, L. fermentum and Staphylococcus aureus], with a few exception [Actinomyces naeslundii, A. viscosus, Streptococcus Group O, Micrococcus luteus and M. citreus]. All gram negative bacteria examined [Proteus mirabilis, Escherichia **coli**, Serratia marcescens, Neisseria perflava, Leptotrichia buccalis and Fusobacterium nucleatum] were free of PGP. The PGP in the hot saline extracts of various gram positive bacteria possessed an

essentially identifical antigenic specificity. The addition of DEAE-Sephadex A-25 resin to hot saline extracts successfully removed the cross-reacting PGP **antigen**. After adsorption of the extract from S. mutans, the supernatant contained only type-specific polysaccharide **antigen**, except type b, in which type b-specific polysaccharide and PGP **antigens** were adsorbed with the resin. This simple procedure should be useful for the removal of the PGP-type teichoic acid from **antigen** extracts of bacteria that contain uncharged polysaccharides.

FILE 'CAPLUS' ENTERED AT 12:18:32 ON 21 JUN 2004
L6 5 S L2 AND INFLUENZA(5A)VIRUS
L7 0 S L6 NOT L3

FILE 'MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, DISSABS, FEDRIP' ENTERED AT 12:19:01 ON 21 JUN 2004
L8 7 S L6
L9 1 S L8 NOT L4

L9 ANSWER 1 OF 1 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
ACCESSION NUMBER: 2003-636770 [60] WPIDS
CROSS REFERENCE: 2003-646091 [61]; 2003-663475 [62]; 2004-098616 [10]
DOC. NO. CPI: C2003-174145
TITLE: Immunogenic composition useful for inducing immune response against tumor, comprising oral formulation of microflora organism having expression vector having heterologous nucleic acid that encodes for **antigen**.
DERWENT CLASS: B04 D16
INVENTOR(S): CHEN, W; FU, X; NOURAINI, S; ZHANG, Z
PATENT ASSIGNEE(S): (SYMB-N) SYMBIGENE INC
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003063785	A2	20030807	(200360)*	EN	82
RW:	AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW				
W:	AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW				
AU 2003210687	A1	20030902	(200422)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003063785	A2	WO 2003-US2468	20030127
AU 2003210687	A1	AU 2003-210687	20030127

FILING DETAILS:

Searcher : Shears 571-272-2528

PATENT NO	KIND	PATENT NO
AU 2003210687	A1 Based on	WO 2003063785

PRIORITY APPLN. INFO: US 2002-401465P 20020805; US
2002-353885P 20020131; US
2002-353923P 20020131; US
2002-353964P 20020131

AN 2003-636770 [60] WPIDS
CR 2003-646091 [61]; 2003-663475 [62]; 2004-098616 [10]
AB WO2003063785 A UPAB: 20040331
NOVELTY - An immunogenic composition (C1) comprising an oral formulation of a microflora organism having an expression vector that comprises a heterologous nucleic acid encoding an **antigen.**

ACTIVITY - Cytostatic; Antibacterial; Virucide; Antiparasitic; Fungicide; Anti-HIV.

MECHANISM OF ACTION - Inducer of immune response (claimed). The immune response inducing activity of (C1) was evaluated by using female Balb/c mice. Six weeks old female Balb/c mice were inoculated by oral, intranasal or subcutaneous routes with yeast displaying VP7, hemagglutinin (HA) or neuraminidase (NA) on the cell surface. Booster inoculations were performed every two weeks. Mice were inoculated with either yeast expressing surface-displayed **antigen** or yeast containing empty vector. Blood samples were collected before the first vaccination (oral: 0.1 ml (5 multiply 108)/mice) and every two weeks thereafter. Mice were sacrificed after 8-weeks. Antibody response were measured by taking blood samples (0.1 ml) from the eye bowl. Serum were separated by centrifugation, and stored at -20 deg. C. The lung and intestine were separated from the sacrificed animal and washed with phosphate buffered saline (PBS). The tissue washings were centrifuged and the supernatants were stored at -20 deg. C. The viral **antigens** VP7, HA or NA were coated on 96 well plates. After blocking of non-specific binding sites, samples of sera, lung or intestine washings were diluted with PBS and added to each well. Horseradish peroxidase-labeled secondary antibodies (anti-IgG or anti-IgA) were used to detect antibody-**antigen** complexes. When compared to the plasmid controls, each immunogenic composition successfully elicited an immune response in the test animal.

USE - (C1) is useful for inducing an immune response in an animal which involves providing (C1) formulated for oral administration to the animal. The **antigen** is chosen from tumors, bacteria, **viruses** (e.g., **influenza**, hepatitis, HIV, and rotavirus), parasites, and fungi. (C1) is useful for inducing an immune response in an animal which involves providing an oral formulation of transformed yeast (S.cerevisiae), where yeast comprise a heterologous nucleic acid encoding for an **antigen** (immunoprotective epitope from influenza A), and the **antigen** is expressed on surface of the yeast (claimed).
Dwg.0/10

(FILE 'MEDLINE' ENTERED AT 12:20:53 ON 21 JUN 2004)
L10 7039 SEA FILE=MEDLINE ABB=ON PLU=ON LACTOBACILLUS/CT
L17 1044 SEA FILE=MEDLINE ABB=ON PLU=ON "ANTIGENS, HETEROPHILE"/

Searcher : Shears 571-272-2528

CT

L18 1 SEA FILE=MEDLINE ABB=ON PLU=ON L10 AND L17

L18 ANSWER 1 OF 1 MEDLINE on STN

ACCESSION NUMBER: 77050628 MEDLINE
DOCUMENT NUMBER: PubMed ID: 825468
TITLE: Selective adsorption of heterophile polyglycerophosphate antigen from antigen extracts of Streptococcus mutans and other gram-positive bacteria.
AUTHOR: Hamada S; Tai S; Slade H D
SOURCE: Infection and immunity, (1976 Oct) 14 (4) 903-10. Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 197701
ENTRY DATE: Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19770128

ED Entered STN: 19900313
Last Updated on STN: 19900313
Entered Medline: 19770128

AB Hot saline extracts of Streptococcus mutans have been shown to contain antigenic substances which occasionally react nonspecifically with some antisera against whole cells of various serological groups and types of streptococci. Chromatography of the extract of S. mutans strain MT703 (serotype e) on a diethylaminoethyl-Sephadex A-25 column gave two principal antigens. One antigen was eluted without adsorption to the resin and was identified as the serotype-specific polysaccharide. The other antigen, which contained a large quantity of phosphorus, was absorbed to and released from the resin by gradient elution. It was reactive against the antisera specific for polyglycerophosphate (PGP) from group A Streptococcus pyogenes and/or S. mutans strain Ingbritt (type c). The PGP antigen was further purified by gel filtration with Sephadex G-75. Two peaks, PGP-1, and PGP-2, were obtained. Each possessed the same antigenic specificity to anti-PGP serum as shown by immunodiffusion. Chemical analyses revealed that the molar ratio of phosphorus to glycerol in both was about 1:1, although the protein content between the two was significantly different. PGP antigen was found to be widely distributed in hot saline extracts from various gram-positive bacteria, with a few exceptions. However, all gram-negative bacteria examined were free of PGP. The PGP in the hot saline extracts of various gram-positive bacteria possessed an essentially identical antigenic specificity. The addition of diethylaminoethyl-Sephadex A-25 resin to hot saline extracts successfully removed the cross-reacting PGP antigen. After adsorption of the extract from S. mutans, the supernatant contained only type-specific polysaccharide antigen, except type b, in which both type b-specific polysaccharide and PGP antigens were absorbed with the resin. This simple procedure should be useful for the removal of the PGP-type teichoic acid from antigen extracts of bacteria that contain uncharged polysaccharides.

Searcher : Shears 571-272-2528

(FILE 'CAPLUS, MEDLINE, BIOSIS, EMBASE, WPIDS, JICST-EPLUS, JAPIO, PHIC, PHIN, TOXCENTER, PASCAL, DISSABS, FEDRIP' ENTERED AT 12:26:11 ON 21 JUN 2004)

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L19        8395 S "SHAW D"?/AU
L20         205 S "LEER R"?/AU
L21         662 S "POUWELS P"?/AU
L22          13 S L19 AND L20 AND L21
L23          13 S L19 AND (L20 OR L21)
L24         121 S L20 AND L21
L25        9128 S L19 OR L20 OR L21
L26          15 S (L24 OR L25) AND L2
L27          20 S L22 OR L23 OR L26
L28           6 DUP REM L27 (14 DUPLICATES REMOVED)
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Author (3)

L28 ANSWER 1 OF 6 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN

ACCESSION NUMBER: 2003-559268 [52] WPIDS
DOC. NO. CPI: C2003-150788
TITLE: New modified bacterial surface layer proteins, useful in vaccines, and in forming crystalline arrays, sheets or layers for binding functional molecules to solid surfaces in biosensors.
DERWENT CLASS: B04 D16
INVENTOR(S): **POUWELS, P H**; SMIT, E; TIELEN, F
PATENT ASSIGNEE(S): (NEDE) TNO NEDERLANDSE ORG TOEGEPAST-NATUURWET; (NEDE) NEDERLANDSE ORG TOEGEPAST
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003055906	A1	20030710	(200352)*	EN	47
RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR IE IT KE LS LU MC MW MZ NL OA PT SD SE SI SK SL SZ TR TZ UG ZM ZW					
W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW					
AU 2002361215	A1	20030715	(200421)		

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003055906	A1	WO 2002-EP14749	20021223
AU 2002361215	A1	AU 2002-361215	20021223

FILING DETAILS:

PATENT NO	KIND	PATENT NO
AU 2002361215	A1 Based on	WO 2003055906

PRIORITY APPLN. INFO: EP 2001-310937 20011228
AN 2003-559268 [52] WPIDS
AB WO2003055906 A UPAB: 20030813

Searcher : Shears 571-272-2528

NOVELTY - A modified bacterial surface layer (S-layer) protein, is new. The modification comprises the internal insertion of a heterologous polypeptide.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a fragment of a bacterial surface layer (S-layer) protein which is:

(a) an N-terminal fragment or a fragment that is capable of forming a dimer with an other such fragment or a trimer with two other such fragments;

(b) capable of forming dimers with another such fragment, and either includes an immunodominant or exposed loop region and is from 20-200 amino acids long; or excludes an entire immunodominant or exposed loop region and is from 20-155 amino acids long;

(2) a polynucleotide encoding a protein defined above;

(3) a vector comprising the polynucleotide;

(4) a host cell comprising or which is has been transformed with the vector;

(5) a bacteria expressing a surface layer protein (or fragment) defined above;

(6) a modified bacteria (other than Lactobacillus casei or Bacillus) which has been modified to express a heterologous S-layer protein;

(7) a L. casei bacterial cell expressing a bacterial S-layer protein that is either not from L. crispatus or is not a collagen binding protein;

(8) a modified bacteria expressing only, or homogeneously, a heterologous or modified S-layer protein;

(9) a vaccine comprising a bacteria above;

(10) a sheet or (optionally crystalline) monolayer or 2-dimensional array comprising several bacterial S-layer proteins, at least one of which is a modified protein defined above;

(11) a solid surface, liquid-air interface, lipid film, liposome or solution comprising a sheet, monolayer or array above;

(12) a solid surface comprising a layer of S-proteins, at least several of which are modified proteins defined above, sandwiched between the surface and a layer of functional molecules; and

(13) a sensor, molecular sieve or ion trap comprising a sheet, layer or array, or a surface defined above.

MECHANISM OF ACTION - Vaccine.

USE - The modified bacterial surface layer proteins and bacteria expressing the modified proteins are useful in vaccines. The modified bacterial surface layer proteins may form crystalline arrays, sheets or layers that can be used to bind functional molecules to solid surfaces in biosensors.

Dwg.0/6

L28 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 1

ACCESSION NUMBER: 2001:207884 CAPLUS

DOCUMENT NUMBER: 134:227335

TITLE: Oral recombinant **Lactobacillus plantarum** vaccines

INVENTOR(S): **Shaw, David Michael; Leer, Robert Jan; Pouwels, Peter**

PATENT ASSIGNEE(S): Nederlandse Organisatie Voor Toegepast-Natuurwetenschappelijk Onderzoek TNO,

Neth.
SOURCE: Eur. Pat. Appl., 19 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1084709	A1	20010321	EP 1999-203056	19990917
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
WO 2001021200	A1	20010329	WO 2000-GB3575	20000918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
EP 1212083	A1	20020612	EP 2000-962689	20000918
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003509469	T2	20030311	JP 2001-524624	20000918
ZA 2002001969	A	20030609	ZA 2002-1969	20020308

PRIORITY APPLN. INFO.: EP 1999-203056 A 19990917
WO 2000-GB3575 W 20000918

AB The present invention relates to an oral vaccine comprising recombinant lactic acid bacteria expressing heterologous **antigen** in vivo intracellularly and/or the surface of the lactic acid bacterium as specific immunogenicity eliciting component for eliciting immunogenicity against the heterologous **antigen**, characterized in that the recombinant lactic acid bacterium is a **Lactobacillus plantarum**. Preferably, the recombinant **Lactobacillus plantarum** comprises an expression vector capable of expressing the heterologous **antigen** intracellularly and/or such that the heterologous **antigen** is exposed on the cell surface under conditions present in the gastrointestinal tract. The recombinant **Lactobacillus plantarum** is preferably a recombinant **Lactobacillus plantarum** 256. The invention also relates to a recombinant **Lactobacillus plantarum**, more specifically a recombinant strain of **Lactobacillus plantarum** 256, for use in the vaccines of the invention; as well as to an expression vector suitable for intracellular expression or exposure of a heterologous **antigen** encoded thereon, said expression vector providing expression in a **Lactobacillus plantarum** of the heterologous **antigen** under conditions existing in the gastrointestinal tract.

REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN

THE RE FORMAT

L28 ANSWER 3 OF 6 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

ACCESSION NUMBER: 2000137432 EMBASE

TITLE: Strain-dependent induction of cytokine profiles in the gut by orally administered Lactobacillus strains.

AUTHOR: Maassen C.B.M.; Van Holten-Neelen C.; Balk F.; Heijne den Bak-Glashouwer M.J.; **Leer R.J.**; Laman J.D.; Boersma W.J.A.; Claassen E.

CORPORATE SOURCE: E. Claassen, Institute Animal Science and Health, ID-LELYSTAD, P.O. Box 65, 8200 AB Lelystad, Netherlands. H.J.H.M.Claassen@id.wag-ur.nl

SOURCE: Vaccine, (22 May 2000) 18/23 (2613-2623).
Refs: 49
ISSN: 0264-410X CODEN: VACCDE

PUBLISHER IDENT.: S 0264-410X(99)00378-3

COUNTRY: United Kingdom

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
030 Pharmacology
037 Drug Literature Index
004 Microbiology
048 Gastroenterology

LANGUAGE: English

SUMMARY LANGUAGE: English

AB Different Lactobacillus strains are frequently used in consumer food products. In addition, recombinant lactobacilli which contain novel expression vectors can now be used in immunotherapeutic applications such as oral vaccination strategies and in T cell tolerance induction approaches for autoimmune disease. Both for food and clinical applications of lactobacilli, proper selection of wild type strains is crucial.For that purpose, eight different common Lactobacillus strains were analysed with respect to mucosal induction of pro- and anti-inflammatory cytokines, IgA-producing plasma cells in the gut, as well as systemic antibody responses against a parenterally administered **antigen**. Immunohistochemical analysis of cytokine-producing cells in the gut villi showed no significant induction of the cytokines IL-1α, IFN-γ, IL-4 or IL-10 after oral administration of wild type Lactobacillus strains. In contrast, oral administration of L. reuteri and L. brevis induced expression of the proinflammatory/Th1 cytokines TNF-α, IL-2 and/or IL-1β. Oral administration of these two strains and L. fermentum also significantly enhanced the IgG response against parenterally administered haptenated chicken gamma globulin (TNP-CGG). The five other strains did not show this adjuvanticity. L. reuteri induced relatively high levels of IgG2a compared to L. murines, a nonadjuving Lactobacillus strain.These findings imply that different Lactobacillus strains induce distinct mucosal cytokine profiles and possess differential intrinsic adjuvanticity. This suggests that rational Lactobacillus strain selection provides a strategy to influence cytokine expression and thereby influence immune responses. Copyright (C) 2000 Elsevier Science Ltd.

L28 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 2
ACCESSION NUMBER: 2000:633042 CAPLUS
DOCUMENT NUMBER: 133:280276
TITLE: Engineering the microflora to vaccinate the mucosa: serum immunoglobulin G responses and activated draining cervical lymph nodes following mucosal application of tetanus toxin fragment C-expressing lactobacilli
AUTHOR(S): **Shaw, D. M.**; Gaerthe, B.; **Leer, R. J.**; Van Der Stap, J. G. M. M.; Smittenaar, C.; Den Bak-Glashouwer, M.-J. Heijne; Thole, J. E. R.; Tielen, F. J.; **Pouwels, P. H.**; Havenith, C. E. G.
CORPORATE SOURCE: TNO-Prevention and Health, Special Program Infectious Diseases, Leiden, 2315 CE, Neth.
SOURCE: Immunology (2000), 100(4), 510-518
CODEN: IMMUAM; ISSN: 0019-2805
PUBLISHER: Blackwell Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB The delivery of **antigens** to mucosal-associated lymphoid tissues in pediatric and immunocompromised populations by safe, non-invasive vectors, such as commensal lactobacilli, represents a crucial improvement to prevailing vaccination options. In this report, the authors describe the oral and nasal immunization of mice with vaccines constructed through an original system for heterologous gene expression in Lactobacillus in which the 50,000-mol. weight (MW) fragment C of tetanus toxin (TTFC) is expressed either as an intracellular or a surface-exposed protein. Our data indicate that **L. plantarum** is more effective in this respect than L. casei and that, under the exptl. conditions investigated, delivery of TTFC expressed as an intracellular **antigen** is more effective than cell-surface expression. Immunization of mice with live recombinant lactobacilli induced significant levels of circulating TTFC-specific IgG following nasal or oral delivery of vaccine strains. In addition, following nasal delivery, secretory IgA (sIgA) was induced in bronchoalveolar lavage fluids, as were **antigen**-specific antibody-secreting cells and **antigen**-specific T-cell activation in draining lymph nodes, substantiating their potential for safe mucosal delivery of pediatric vaccines.
REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 3
ACCESSION NUMBER: 1999:318971 CAPLUS
DOCUMENT NUMBER: 131:143204
TITLE: Instruments for oral disease-intervention strategies: recombinant Lactobacillus casei expressing tetanus toxin fragment C for vaccination or myelin proteins for oral tolerance induction in multiple sclerosis
AUTHOR(S): Maassen, C. B. M.; Laman, J. D.; Den Bak-Glashouwer, M. J. Heijne; Tielen, F. J.; Van Holten-Neelen, J. C. P. A.; Hoogteijling, L.;

Antonissen, C.; **Leer, R. J.**; **Pouwels, P. H.**; Boersma, W. J. A.; **Shaw, D. M.**
CORPORATE SOURCE: Division of Immunological and Infectious Diseases, TNO-Prevention and Health (TNO-PG), Leiden, 2301 CE, Neth.
SOURCE: Vaccine (1999), 17(17), 2117-2128
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Lactobacillus strains possess properties that make them attractive candidates as vehicles for oral administration of therapeutics. In this report we describe the construction and anal. of recombinant Lactobacillus casei applicable in oral vaccination against an infectious disease (tetanus) and in oral tolerance induction for intervention in an autoimmune disease, multiple sclerosis. Recombinant L. casei which express surface-anchored tetanus toxin fragment C (TTFC) were generated. Quant. anal. by flow cytometry demonstrated a high level of cell wall-bound expression of TTFC and immunogenicity was demonstrated by parenteral immunization with whole cell exts. of the recombinants. A series of expression vectors was constructed to secrete human myelin basic protein (hMBP) or hMBP as a fusion protein with β-glucuronidase from Escherichia coli. These heterologous products produced by L. casei were detected in the growth medium and parenteral immunization with this medium evoked antibodies against hMBP, confirming that secretion indeed had occurred. Based on the different localization of the heterologous proteins, lactobacilli expressing surface-anchored TTFC are ideally suited for the induction of antibody responses, whereas lactobacilli that secrete myelin proteins can be used for the induction of peripheral T-cell tolerance. In conclusion, the specific technol. described here allows the construction of a wide array of safe live recombinant lactobacilli which may prove to be useful in oral intervention strategies for the prevention of infectious diseases or treatment of autoimmune diseases.
REFERENCE COUNT: 31 THERE ARE 31 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L28 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2004 ACS on STN DUPLICATE 4
ACCESSION NUMBER: 1996:76985 CAPLUS
DOCUMENT NUMBER: 124:143041
TITLE: The potential of Lactobacillus as a carrier for oral immunization: Development and preliminary characterization of vector systems for targeted delivery of **antigens**
AUTHOR(S): **Pouwels, Peter H.**; **Leer, Rob J.**; Boersma, Wim J. A.
CORPORATE SOURCE: TNO Nutrition and Food Research Institute, Molecular Genetics and Gene Technology, P.O. Box 5815, HV Rijswijk, 2280, Neth.
SOURCE: Journal of Biotechnology (1996), 44(1-3), 183-92
CODEN: JBITD4; ISSN: 0168-1656
PUBLISHER: Elsevier

DOCUMENT TYPE: Journal
LANGUAGE: English

AB Oral administration of lactobacilli evokes mucosal and systemic immune responses against epitopes associated with these organisms (Gerritse et al., 1990, 1991). The adjuvant function of different Lactobacillus species was investigated under the conditions of i.p. injection or oral administration. After i.p. injection of trinitrophenylated chicken γ-globulin, high DTH responses were observed with Lactobacillus casei and **Lactobacillus plantarum**, but low responses with Lactobacillus fermentum and Lactobacillus delbrueckii subsp. bulgaricus. In different exptl. model systems L. casei and **L. plantarum** consistently showed significant adjuvanticity. A series of expression and expression-secretion vectors containing the strong constitutive promoter of the L. casei L-ldh gene or the regulatable promoter of the Lactobacillus amylovorus amy gene (Pouwels and Leer, 1995) was used for the intracellular, extracellular and surface-bound expression of an influenza virus antigenic determinant fused to Escherichia coli β-glucuronidase. Intracellular expression of the fusion protein amounted to 1-2% of total soluble protein. Lactobacilli synthesizing the fusion protein intracellularly evoked an oral immune response after s.c. priming.

FILE 'HOME' ENTERED AT 12:27:58 ON 21 JUN 2004

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10/088341

21jun04 12:12:55 User219783 Session D2027.3

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File 357:DERWENT BIOTECH RES. _1982-2004/JUN W3
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Set Items Description
S1 105 (LACTOBACILLUS OR L)(W)PLANTARUM AND ANTIGEN? ?
S2 73 S1 AND (INFLUENZA(5N)VIRUS? OR COLI)
S3 25 RD (unique items)
>>>No matching display code(s) found in file(s): 65, 113

- key terms

3/3,AB/1 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)
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18385557 Document Delivery Available: 000221120100025 References: 45
TITLE: Pattern of cytokine responses to gram-positive and gram-negative commensal bacteria is profoundly changed when monocytes differentiate into dendritic cells
AUTHOR(S): Karlsson H (REPRINT); Larsson P; Wold AE; Rudin A
AUTHOR(S) E-MAIL: helen.karlsson@immuno.gu.se
CORPORATE SOURCE: Gothenburg Univ, Dept Rheumatol & Inflammat Res, Guldhedsgatan 10A/S-41346 Gothenburg//Sweden/ (REPRINT); Gothenburg Univ, Dept Rheumatol & Inflammat Res, /S-41346 Gothenburg//Sweden/; Gothenburg Univ, Dept Clin Bacteriol, /S-41346 Gothenburg//Sweden/
PUBLICATION TYPE: JOURNAL
PUBLICATION: INFECTION AND IMMUNITY, 2004, V72, N5 (MAY), P2671-2678
GENUINE ARTICLE#: 816OV
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
ISSN: 0019-9567
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The normal gastrointestinal bacterial flora is crucial for the maturation of acquired immunity via effects on **antigen**-presenting cells (APCs). Here we investigated how two types of APCs, monocytes and dendritic cells (DCs), react to different bacterial strains typical of the commensal intestinal microflora. Purified human monocytes and monocyte-derived DCs were stimulated with LTV-inactivated gram-positive (**Lactobacillus plantarum** and Bifidobacterium adolescentis) and gram-negative (Escherichia **coli** and Veillonella parvula) bacterial strains. Monocytes produced higher levels of interleukin 12p70 (IL-12p70) and tumor necrosis factor (TNF), as detected by an enzyme-linked immunosorbent assay, in response to **L. plantarum** than in

response to E. **coli** and V. parvuld. In contrast, DCs secreted large amounts of IL-12p70, TNF, IL-6, and IL-10 in response to E. **coli** and V. parvuld but were practically unresponsive to **L. plantarum** and B. adolescentis. The lack of a response to the gram-positive strains correlated with lower surface expression of Toll-like receptor 2 (TLR2) on DCs than on monocytes. The surface expression of TLR4 on DCs was undetectable when it was analyzed by flow cytometry, but blocking this receptor decreased the TNF production in response to V. parvula, indicating that TLR4 is expressed at a low density on DCs. Gamma interferon increased the expression of TLR4 on DCs and also potentiated the cytokine response to the gram-negative strains. Our results indicate that when monocytes differentiate into DCs, their ability to respond to different commensal bacteria dramatically changes, and they become unresponsive to probiotic gram-positive bacteria. These results may have important implications for the abilities of different groups of commensal bacteria to regulate mucosal and systemic immunity.

3/3,AB/2 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

15589155 Document Delivery Available: 000180787600003 References: 42
TITLE: Lactic acid bacteria isolated from dairy products inhibit genotoxic effect of 4-nitroquinoline-1-oxide in SOS-chromotest
AUTHOR(S): Cenci G (REPRINT); Rossi J; Trotta F; Caldini G
AUTHOR(S) E-MAIL: gcenci@unipg.it
CORPORATE SOURCE: Univ Perugia, Dipartimento Biol Cellulare & Mol, Via Giochetto/I-06126 Perugia//Italy/ (REPRINT); Univ Perugia, Dipartimento Biol Cellulare & Mol, /I-06126 Perugia//Italy/; Univ Perugia, Dipartimento Sci Alimenti, /I-06126 Perugia//Italy/
PUBLICATION TYPE: JOURNAL
PUBLICATION: SYSTEMATIC AND APPLIED MICROBIOLOGY, 2002, V25, N4 (DEC), P 483-490
GENUINE ARTICLE#: 642CW
PUBLISHER: URBAN & FISCHER VERLAG, BRANCH OFFICE JENA, P O BOX 100537, D-07705 JENA, GERMANY
ISSN: 0723-2020
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Antigenotoxic activity against 4-nitroquinoline-1-oxide (4-NQO) of lactic acid bacteria isolated from commercial dairy products was studied using SOS-Chromotest. The supernatants from bacteria-genotoxin co-incubations in general exhibited a strong suppression on SOS-induction produced by 4-NQO on the tester organism Escherichia **coli** PQ37 (sfiA:lacZ). High genotoxicity inhibition (>75%) was found for 31/67 of the examined bacteria and the maximum values of some strains within the species were as follows: Lactobacillus casei, 99.1%; **L. plantarum**, 93.3%; L. rhamnosus, 93.4%; L. acidophilus, 90.9%; L. delbrueckii subsp. bulgaricus, 85.7% and Bifidobacterium bifidum, 89.6%; Strains with low **antigeno**-toxicity (5-60%) were evidenced in both L. acidophilus and L. delbrueckii subsp. bulgaricus, whereas some inactive strains were found only in L. casei and L. delbrueckii subsp. bulgaricus. Cell exposure to 100 degreesC for 15 min prevented antigenotoxicity and no effect was evidenced for cell-free spent media. The active strains survived at 0.1 mM 4-NQO exposure and generally presented some relevant functional properties, such

as tolerance to bile (0.5%) or acid environment (pH 2.0) and adherence to Caco-2 enterocytes. Antigenotoxicity was always associated with modification of the 4-NQO absorbance profile.

3/3,AB/3 (Item 3 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

12040991 References: 39
TITLE: Adaptation of the nisin-controlled expression system in **Lactobacillus plantarum**: a tool to study in vivo biological effects
AUTHOR(S): Pavan S; Hols P; Delcour J; Geoffroy MC; Grangette C; Kleerebezem M; Mercenier A (REPRINT)
AUTHOR(S) E-MAIL: annick.mercenier@pasteur-lille.fr
CORPORATE SOURCE: Inst Pasteur, Dept Microbiol Ecosyst, 1 Rue Pr Calmette,BP 245/F-59019 Lille//France/ (REPRINT); Inst Pasteur, Dept Microbiol Ecosyst, /F-59019 Lille//France/; Univ Catholique Louvain, Unite Genet, /B-1348 Louvain//Belgium/; NIZO Food Res, Wageningen Ctr Food Sci, /NL-6710 BA Ede//Netherlands/
PUBLICATION TYPE: JOURNAL
PUBLICATION: APPLIED AND ENVIRONMENTAL MICROBIOLOGY, 2000, V66, N10 (OCT), P4427-4432
GENUINE ARTICLE#: 360CW
PUBLISHER: AMER SOC MICROBIOLOGY, 1752 N ST NW, WASHINGTON, DC 20036-2904 USA
ISSN: 0099-2240
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: The potential of lactic acid bacteria as live vehicles for the production and delivery of therapeutic molecules is being actively investigated today. For future applications it is essential to be able to establish dose-response curves for the targeted biological effect and thus to control the production of a heterologous biopeptide by a live lactobacillus. We therefore implemented in **Lactobacillus plantarum** NCIMB8826 the powerful nisin-controlled expression (NICE) system based on the autoregulatory properties of the bacteriocin nisin, which is produced by Lactococcus lactis. The original two-plasmid NICE system turned out to be poorly suited to **L. plantarum**. In order to obtain a stable and reproducible nisin dose-dependent synthesis of a reporter protein (P-glucuronidase) or a model **antigen** (the C subunit of the tetanus toxin, TTFC), the lactococcal nisRK regulatory genes were integrated into the chromosome of **L. plantarum** NCIMB8826. Moreover, recombinant **L. plantarum** producing increasing amounts of TTFC was used to establish a dose-response curve after subcutaneous administration to mice. The induced serum immunoglobulin G response was correlated with the dose of **antigen** delivered by the live lactobacilli.

3/3,AB/4 (Item 4 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

11224126 References: 38
TITLE: Use of green fluorescent protein to tag lactic acid bacterium

strains under development as live vaccine vectors
AUTHOR(S): Geoffroy MC; Guyard C; Quatannens B; Pavan S; Lange M; Mercenier A (REPRINT)
AUTHOR(S) E-MAIL: annick.mercenier@pasteur-lille.fr
CORPORATE SOURCE: Inst Pasteur, Dept Microbiol Ecosyst, 1 Rue Pr Calmette,BP 245/F-59019 Lille//France/ (REPRINT); Inst Pasteur, Dept Microbiol Ecosyst, /F-59019 Lille//France/; Inst Biol, UMR 3586, /F-59019 Lille//France/
PUBLICATION TYPE: JOURNAL
PUBLICATION: APPLIED AND ENVIRONMENTAL MICROBIOLOGY, 2000, V66, N1 (JAN), P 383-391
GENUINE ARTICLE#: 271GL
PUBLISHER: AMER SOC MICROBIOLOGY, 1325 MASSACHUSETTS AVENUE, NW, WASHINGTON, DC 20005-4171 USA
ISSN: 0099-2240
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: The lactic acid bacteria (LAB) are safe microorganisms which are mainly used for the preparation of fermented foods and for probiotic applications, The potential of LAB as live vehicles for the production and delivery of therapeutic molecules such as **antigens** is also being actively investigated today. However, very little is known about the fate of live LAB when administered in vivo and about the interaction of these microorganisms with the nasal or gastrointestinal ecosystem, For future applications, it is essential to be able to discriminate the biotherapeutic strain from the endogenous microflora and to unravel the mechanisms underlying the postulated health-beneficial effect. We therefore started to investigate both aspects in a mouse model with two LAB species presently under development as live vaccine vectors, i.e., Lactococcus lactis and **Lactobacillus plantarum**. We have constructed different expression vectors carrying the gfp (green fluorescent protein [GFP]) gene from the jellyfish Aequoria victoria, and we found that this visible marker was best expressed when placed under the control of the inducible strong nisA promoter from L. lactis. Notably, a threshold amount of GFP was necessary to obtain a bright fluorescent phenotype. We further demonstrated that fluorescent **L, plantarum** NCIMB8826 can be enumerated and sorted by flow cytometry. Moreover, tagging of this strain with GFP allowed us to visualize its phagocytosis by macrophages in vitro and ex vivo and to trace it in the gastrointestinal tract of mice upon oral administration.

3/3,AB/5 (Item 5 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

10732053 References: 34
TITLE: Immunomodulatory effects of **Lactobacillus plantarum** colonizing the intestine of gnotobiotic rats
AUTHOR(S): Herias MV (REPRINT); Hessle C; Telemo E; Midtvedt T; Hanson LA; Wold AE
AUTHOR(S) E-MAIL: v.herias@immuno.gu.se
CORPORATE SOURCE: Gothenburg Univ, Dept Clin Immunol, Guldhedsgatan 10/S-41346 Gothenburg//Sweden/ (REPRINT); Gothenburg Univ, Dept Clin Immunol, /S-41346 Gothenburg//Sweden/; Karolinska Inst, Dept Med Microbial Ecol, /S-10401 Stockholm//Sweden/
PUBLICATION TYPE: JOURNAL

PUBLICATION: CLINICAL AND EXPERIMENTAL IMMUNOLOGY, 1999, V116, N2 (MAY), P 283-290
GENUINE ARTICLE#: 215HF
PUBLISHER: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND
ISSN: 0009-9104
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: We have studied the effect of the probiotic strain **Lactobacillus plantarum** 299v on the immune functions of gnotobiotic rats. One group of germ-free rats was colonized with the type 1-fimbriated Escherichia **coli** O6: K13:H1 and another group with the same E. **coli** strain together with **L. plantarum** 299v. One and 5 weeks after colonization, bacterial numbers were determined in the contents of the small intestine, caecum and mesenteric lymph nodes. Small intestinal sections were examined for CD8(+), CD4(+), CD25(+) (IL-2R alpha-chain), IgA(+) and MHC class II+ cells and mitogen-induced spleen cell proliferation was determined. Immunoglobulin levels and E. **coli** -specific antibodies were measured in serum. Rats given **L. plantarum** in addition to E. **coli** showed lower counts of E. **coli** in the small intestine and caecum 1 week after colonization compared with the group colonized with E. **coli** alone, but similar levels after 5 weeks. Rats colonized with **L. plantarum** + E. **coli** had significantly higher total serum IgA levels and marginally higher IgM and IgA antibody levels against E. **coli** than those colonized with E. **coli** alone. They also showed a significantly increased density of CD25(+) cells in the lamina propria and displayed a decreased proliferative spleen cell response after stimulation with concanavalin A or E. **coli** 1 week after colonization. The results indicate that **L. plantarum** colonization competes with E. **coli** for intestinal colonization and can influence intestinal and systemic immunity.

3/3,AB/6 (Item 6 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

08727328 References: 48
TITLE: Efficient secretion of the model **antigen** M6-gp41E in **Lactobacillus plantarum** NCIMB 8826
AUTHOR(S): Hols P; Slos P; Dutot P; Reymund J; Chabot P; Delplace B; Delcour J (REPRINT); Mercenier A
CORPORATE SOURCE: UNIV CATHOLIQUE LOUVAIN,GENET UNIT, 5 PL CROIX SUD/B-1348 LOUVAIN//BELGIUM/ (REPRINT); UNIV CATHOLIQUE LOUVAIN,GENET UNIT/B-1348 LOUVAIN//BELGIUM/; TRANSGENE SA,/F-67082 STRASBOURG//FRANCE/
PUBLICATION TYPE: JOURNAL
PUBLICATION: MICROBIOLOGY-UK, 1997, V143, ,8 (AUG), P2733-2741
GENUINE ARTICLE#: XQ875
PUBLISHER: SOC GENERAL MICROBIOLOGY, MARLBOROUGH HOUSE, BASINGSTOKE RD, SPENCERS WOODS, READING, BERKS, ENGLAND RG7 1AE
ISSN: 1350-0872
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Four Lactobacillus strains (Lb. plantarum NCIMB 8826, Lb. paracasei LbTGS1.4, Lb. casei ATCC 393 and Lb. fermentum KLD) were tested

for their ability to produce and secrete heterologous proteins. These strains were first screened with an a-amylase reporter under the control of a set of expression or expression/secretion signals from various lactic acid bacteria. With most of the constructions tested, the lever of extracellular production was highest in Lb. plantarum NCIMB 8826, and lowest in Lb. paracasei LbTGS1.4. These two strains were next assayed using a model **antigen** consisting of the N-terminal part of the M6 protein from Streptococcus pyogenes fused to the linear epitope ELDKWAS from human immunodeficiency virus gp41 protein. Secretion of this heterologous protein was inefficient in Lb. paracasei LbTGS1.4 which accumulated a large intracellular pool of the unprocessed precursor. whereas Lb. plantarum NCIMB 8826 was able to secrete the **antigen** to a revel as high as 10 mg l(-1).

3/3,AB/7 (Item 7 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

08082800 References: 23
TITLE: T cell receptor-alpha beta-deficient mice fail to develop colitis in the absence of a microbial environment
AUTHOR(S): Dianda L; Hanby AM; Wright NA; Sebesteny A; Hayday AC; Owen MJ (REPRINT)
CORPORATE SOURCE: IMPERIAL CANC RES FUND,44 LINCOLNS INN FIELDS/LONDON WC2A 3PX//ENGLAND/ (REPRINT); IMPERIAL CANC RES FUND,/LONDON WC2A 3PX//ENGLAND/; YALE UNIV,DEPT BIOL/NEW HAVEN//CT/
PUBLICATION TYPE: JOURNAL
PUBLICATION: AMERICAN JOURNAL OF PATHOLOGY, 1997, V150, N1 (JAN), P91-97
GENUINE ARTICLE#: WB761
PUBLISHER: AMER SOC INVESTIGATIVE PATHOLOGY, INC, 428 EAST PRESTON ST, BALTIMORE, MD 21202-3993
ISSN: 0002-9440
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Mice with null mutations in cytokine or T cell receptor (TCR) genes develop intestinal inflammation. In the case of interleukin-2(-/-) and interleukin-10(-/-) mice it has been demonstrated that normal intestinal bacterial flora can cause gut pathology. TCR-alpha(-/-) mice not only develop colitis but also produce a strong antibody response to self-**antigens**, such as double-stranded DNA. It is therefore important to establish whether the intestinal inflammation develops spontaneously or is induced by luminal **antigens**. To address this issue, a germ-free colony of TCR-alpha(-/-) mice was derived and compared with TCR-alpha(-/-) mice kept in conventional specific-pathogen-free conditions. Although specific-pathogen-free animals developed colitis with a high level of penetrance, there was no evidence of intestinal pathology in germ-free animals. Furthermore, intestinal inflammation was not seen in TCR-alpha(-/-) mice colonized With a limited bacterial flora consisting of **Lactobacillus plantarum**, Streptococcus faecalis, S. faecium, and/or Escherichia **coli** We conclude that intestinal inflammation in TCR-alpha(-/-) mice does not occur spontaneously nor does it result from the presence of bacteria, per se, but rather it is initiated by a specific organism or group of organisms normally present in the gut flora that hare yet to be identified.

3/3,AB/8 (Item 8 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

07123625 References: 27
TITLE: THE POTENTIAL OF LACTOBACILLUS AS A CARRIER FOR ORAL IMMUNIZATION - DEVELOPMENT AND PRELIMINARY CHARACTERIZATION OF VECTOR SYSTEMS FOR TARGETED DELIVERY OF **ANTIGENS**
AUTHOR(S): POUWELS PH; LEER RJ; BOERSMA WJA
CORPORATE SOURCE: TNO,NUTR & FOOD RES INST,POB 5815/2280 HV RIJSWIJK//NETHERLANDS/ (Reprint); TNO,DIV INFECT DIS & IMMUNOL/2301 CE LEIDEN//NETHERLANDS/
PUBLICATION: JOURNAL OF BIOTECHNOLOGY, 1996, V44, N1-3 (JAN 26), P183-192
GENUINE ARTICLE#: TU634
ISSN: 0168-1656
LANGUAGE: ENGLISH DOCUMENT TYPE: ARTICLE

ABSTRACT: Oral administration of lactobacilli evokes mucosal and systemic immune responses against epitopes associated with these organisms (Gerritse et al., 1990, 1991). The adjuvant function of different Lactobacillus species was investigated under the conditions of intraperitoneal (i.p.) injection or oral administration. After i.p. injection of trinitrophenylated chicken gamma-globulin, high DTH responses were observed with Lactobacillus casei and **Lactobacillus plantarum**, but low responses with Lactobacillus fermentum and Lactobacillus delbrueckii subsp. bulgaricus. In different experimental model systems L. casei and **L. plantarum** consistently showed significant adjuvanticity. A series of expression and expression-secretion vectors containing the strong constitutive promoter of the L. casei L-ldh gene or the regulatable promoter of the Lactobacillus amylovorus amy gene (Pouwels and Leer, 1995) was used for the intracellular, extracellular and surface-bound expression of an **influenza virus** antigenic determinant fused to Escherichia **coli** P-glucuronidase, Intracellular expression of the fusion protein amounted to 1-2% of total soluble protein. Lactobacilli synthesizing the fusion protein intracellularly evoked an oral immune response after subcutaneous priming.

3/3,AB/9 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01563209
A method for testing the effect of nutrients on gastrointestinal colonisation resistance of humans
Verfahren zur Prufung der Wirkung von Nahrungsmittel, eine Resistenz gegen Kolonisation durch Bakterien zuerzeugen
Methode d'analyse de la resistence envers une colonisation des intenstins cause par l'alimentation
PATENT ASSIGNEE:
Stichting Top-Instituut Voedselwetenschappen, (3270561), Diedenweg 20, P.O. Box 557, 6700 AN Wageningen, (NL), (Applicant designated States: all)
INVENTOR:
Bodee-Oudenhoven, Ingeborg Marie Jacqueline, Saltshof 3020, 6604 GL

Wijchen, (NL)
Van der Meer, Roelof, Witte de Withstraat 37, 6712 HA Ede, (NL)
LEGAL REPRESENTATIVE:
van Westenbrugge, Andries et al (62593), Nederlandsch Octrooibureau P.O. Box 29720, 2502 LS The Hague, (NL)
PATENT (CC, No, Kind, Date): EP 1300472 A1 030409 (Basic)
APPLICATION (CC, No, Date): EP 2001203745 011002;
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE; TR
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12Q-001/10; G01N-033/569

ABSTRACT EP 1300472 A1
The present invention relates to a method for testing the effect of a substance, in particular a food-ingredient, on the resistance to microbial infection of the human gastrointestinal tract. The microorganism may be a gastrointestinal pathogen, such as a virus, a bacterium, a fungus or a protozoan organism, in which case usually a attenuated or non-virulent strain of the microorganism, such as a live oral vaccine, will be applied in the method . Alternatively, the method may be applied to test the effect of the substance on the capability of non-pathogenic beneficial bacterium to colonise the intestinal mucosa. In a specific example, the method demonstrates that calcium reduces the severity of infection by an enterotoxigenic E.**coli** as well as the clinical symptoms associated with the infection. In a further aspect the invention therefore relates to a method for preventing or reducing the severity of a gastrointestinal infection by a Gram-negative pathogenic bacterium by increasing the gastrointestinal calcium concentration.
ABSTRACT WORD COUNT: 159
NOTE:
Figure number on first page: 1

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200315	551
SPEC A	(English)	200315	3510
Total word count - document A			4061
Total word count - document B			0
Total word count - documents A + B			4061

3/3,AB/10 (Item 2 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01510603
Compositions and methods for human gastrointestinal health
Zusammensetzungen und Methoden welche der humanen gastrointestinalen Gesundheit dienen
Compositions et methodes benefiques a la sante humaine dans l'appareil gastro-intestinal
PATENT ASSIGNEE:
METAGENICS, INC., (1756180), 971 Calle Negocio, San Clemente, CA 92672, (US), (Applicant designated States: all)
INVENTOR:

Paul, Stephen M., 16 Optima, San Clemente, California 92672, (US)
LEGAL REPRESENTATIVE:
Thomson, Paul Anthony et al (36701), Potts, Kerr & Co. 15, Hamilton Square, Birkenhead Merseyside CH41 6BR, (GB)
PATENT (CC, No, Kind, Date): EP 1262192 A2 021204 (Basic)
EP 1262192 A3 030205
APPLICATION (CC, No, Date): EP 2002014291 951027;
PRIORITY (CC, No, Date): US 331140 941028; US 437316 950509
DESIGNATED STATES: BE; DK; FR; GB; NL; SE
RELATED PARENT NUMBER(S) - PN (AN):
EP 787006 (EP 95938934)
INTERNATIONAL PATENT CLASS: A61K-035/00; A61K-035/20; A61K-039/02; A61K-039/07; A61K-039/395; A61K-039/40; A61K-039/42; A61K-047/00

ABSTRACT EP 1262192 A2
A composition for promoting gastrointestinal health comprises an effective amount of a beneficial human intestinal microorganism and an effective amount of an immunoglobulin composition comprising concentrated immunologically active immunoglobulins. Preferred beneficial human intestinal microoganisms include lactobacilli and bifidobacteria. The immunologically active immunoglobulins are preferably purified from bovine milk, milk products, or whey. Methods of use are also described.
ABSTRACT WORD COUNT: 59
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200249	371
SPEC A	(English)	200249	9145
Total word count - document A			9516
Total word count - document B			0
Total word count - documents A + B			9516

3/3,AB/11 (Item 3 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01500185
PROCESS FOR PRODUCING PRENYL ALCOHOL
VERFAHREN ZUR HERSTELLUNG VON PRENYLALKOHOL
PROC D DE PRODUCTION D'ALCOOL PR NYLE
PATENT ASSIGNEE:
TOYOTA JIDOSHA KABUSHIKI KAISHA, (203744), 1, Toyota-cho, Toyota-shi, Aichi 471-8571, (JP), (Applicant designated States: all)
INVENTOR:
OHTO, Chikara, c/o Toyota Jidosha KK, 1, Toyota-cho, Toyota-shi, Aichi 471-8571, (JP)
OBATA, Shusei, c/o Toyota Jidosha KK, 1, Toyota-cho, Toyota-shi, Aichi 471-8571, (JP)
MURAMATSU, Masayoshi, c/o Toyota Jidosha KK, 1, Toyota-cho, Toyota-shi, Aichi 471-8571, (JP)
NISHI, Kiyohiko, c/o Ajinomoto Co.,Inc., 450, Oaza-Morodomitsu, Morodomi-cho, Saga-gun, Saga 840-2193, (JP)

TOTSUKA, Kazuhiko, c/o Ajinomoto Co.,Inc., 15-1, Kyobashi 1-chome, Chuo-ku, Tokyo 104-8315, (JP)
LEGAL REPRESENTATIVE:
Leson, Thomas Johannes Alois, Dipl.-Ing. et al (78982), Tiedtke-Buhling-Kinne & Partner GbR, TBK-Patent, Bavariaring 4, 80336 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1354955 A1 031022 (Basic)
WO 2002053746 020711
APPLICATION (CC, No, Date): EP 2001272514 011220; WO 2001JP11214 011220
PRIORITY (CC, No, Date): JP 2000403067 001228
DESIGNATED STATES: DE; FR; GB
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12N-015/52; C12P-007/04; C12N-001/19; C12N-001/21

ABSTRACT EP 1354955 A1
A method of producing a prenyl alcohol, comprising creating a recombinant by transferring into a host a recombinant DNA for expression or a DNA for genomic integration each comprising a prenyl diphosphate synthase gene or a mutant thereof, culturing the resultant recombinant, and recovering the prenyl alcohol from the resultant culture.
ABSTRACT WORD COUNT: 52
NOTE:
Figure number on first page: 038

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200343	1557
SPEC A	(English)	200343	24846
Total word count - document A			26403
Total word count - document B			0
Total word count - documents A + B			26403

3/3,AB/12 (Item 4 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01267301
Continuous fermentation process
Kontinuierliches Fermentationsverfahren
Procede de fermentation en continu
PATENT ASSIGNEE:
DSM IP Assets B.V., (4438030), Het Overloon 1, 6411 TE Heerlen, (NL), (Applicant designated States: all)
INVENTOR:
Bartok, Attila, Rieterplatz 5, 8002 Zurich, (CH)
Muh, Thorsten, Am blauen Berg 6, 51375 Leverkusen, (DE)
Ruckel, Markus, Birkenstrasse 25, 82377 Penzberg, (DE)
LEGAL REPRESENTATIVE:
Keller, Gunter, Dr. et al (59792), Lederer & Keller Patentanwalte Prinzregentenstrasse 16, 80538 Munchen, (DE)
PATENT (CC, No, Kind, Date): EP 1092764 A2 010418 (Basic)
EP 1092764 A3 040317
APPLICATION (CC, No, Date): EP 2000121663 001004;

PRIORITY (CC, No, Date): EP 99120289 991011; EP 2000119676 000908
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12M-001/36

ABSTRACT EP 1092764 A2
The invention is concerned with a continuous process for the manufacture of proteins by means of protein-producing microorganism in which process the microorganism is optionally immobilized on a solid carrier and/or the nutrients and other agents required for the growth of the microorganism and the optimal production of protein are fed into the reactor individually at a constant dilution rate. Furthermore, the invention is concerned with a process for the manufacture of proteins using a fermentation assembly.
ABSTRACT WORD COUNT: 78
NOTE:
Figure number on first page: 1

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200116	699
SPEC A	(English)	200116	10625
Total word count - document A			11324
Total word count - document B			0
Total word count - documents A + B			11324

3/3,AB/13 (Item 5 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01258934
Oral recombinant lactobacilli vaccines
Oraler Impfstoff enthaltend rekombinanten Lactobacilli
Vaccin oral contenant des Lactobacilli recombines
PATENT ASSIGNEE:
NEDERLANDSE ORGANISATIE VOOR TOEGEPAST-NATUURWETENSCHAPPELIJK ONDERZOEK TNO, (285526), Schoemakerstraat 97, P.O. Box 60680, 2628 VK Delft, (NL), (Applicant designated States: all)
INVENTOR:
Shaw, David, Michael, 18 Austins-Mead, HP3 OJX Bovingdon, Hertfordshire, (GB)
Leer, Robert Jan, Kompas 7, 3904 PN Veenendaal, (NL)
Pouwels, Peter, Delftweg 14, 2289 AJ Rijswijk, (NL)
LEGAL REPRESENTATIVE:
Wright, Simon Mark et al (72652), J.A. Kemp & Co. 14 South Square Gray's Inn, London WC1R 5LX, (GB)
PATENT (CC, No, Kind, Date): EP 1084709 A1 010321 (Basic)
EP 1084709 A9 010516
APPLICATION (CC, No, Date): EP 99203056 990917;
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-039/00; C12N-015/74

ABSTRACT EP 1084709 A1

The present invention relates to an oral vaccine comprising recombinant lactic acid bacteria expressing heterologous **antigen** in vivo intracellularly and/or the surface of the lactic acid bacterium as specific immunogenicity eliciting component for eliciting immunogenicity against the heterologous **antigen**, characterised in that the recombinant lactic acid bacterium is a **Lactobacillus plantarum**.

Preferably, the recombinant **Lactobacillus plantarum** comprises an expression vector capable of expressing the heterologous **antigen** intracellularly and/or such that the heterologous **antigen** is exposed on the cell surface under conditions present in the gastrointestinal tract.

The recombinant **Lactobacillus plantarum** is preferably a recombinant **Lactobacillus plantarum** 256.

The invention also relates to a recombinant **Lactobacillus plantarum**, more specifically a recombinant strain of **Lactobacillus plantarum** 256, for use in the vaccines of the invention; as well as to an expression vector suitable for intracellular expression or exposure of a heterologous **antigen** encoded thereon, said expression vector providing expression in a **Lactobacillus plantarum** of the heterologous **antigen** under conditions existing in the gastrointestinal tract.

ABSTRACT WORD COUNT: 163

NOTE:

Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English

FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	200112	808
SPEC A	(English)	200112	10117
Total word count - document A			10925
Total word count - document B			0
Total word count - documents A + B			10925

3/3,AB/14 (Item 6 from file: 348)

DIALOG(R)File 348:EUROPEAN PATENTS

01087165

Oral product for the prevention and therapy of porcine gastroenteric infections

Orales Produkt zur Vorbeugung und Therapie von gastroenterischen Infektionen bei Schweinen

Produit oral pour la prevention et la therapie des infections gastrointeriques porcines

PATENT ASSIGNEE:

Medipharm CZ, s.r.o., (2607110), Starovice 215, P O Box 28, 693 01 Hustopece u Brna, (CZ), (Applicant designated States: all)

INVENTOR:

Mican, Petr, Hradni 43, 693 01 Hustopece u Brna, (CZ)

Stepanek, Jan, Olesinky 14, 592 56 Zvole nad Perstynem, (CZ)

LEGAL REPRESENTATIVE:

McCallum, Graeme David et al (76222), Lloyd Wise, McNeight & Lawrence, Regent House, Heaton Lane, Stockport, Cheshire SK4 1BS, (GB)
PATENT (CC, No, Kind, Date): EP 955061 A1 991110 (Basic)
APPLICATION (CC, No, Date): EP 99301120 990216;
PRIORITY (CC, No, Date): CZ 98859 980320
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; IT; LI; NL; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-039/40; A61K-039/42; A61K-035/74; A61K-031/07; A61K-031/355; A61K-031/59; A61K-039/42; A61K-39:40; A61K-35:74; A61K-039/42; A61K-39:40; A61K-31:07; A61K-31:355; A61K-31:59

ABSTRACT EP 955061 A1

Oral product for the prevention and therapy of porcine gastrointestoinal infections containing at least one specific antibody to porcine rotavirus, porcine coronavirus, enteropathogenic and enterotoxigenic bacterial strains of Escherichia **coli**, Clostridium sp., Salmonella sp. and protozoan strains of Isospora sp. and Cryptosporidium sp, obtained from egg yolks of immunized hens. Further, the product contains at least one strain of live stabilized cultures of lactacidogenic bacteria. Technology of production consisting of separate submersive culture of selected individual strains of lactacidogenic bacterial species Enterococcus faecium, Lactobacillus casei and, if appropriate, **Lactobacillus plantarum**, followed by the separation of the bacterial cells from the medium, their preservation by freeze-drying, and in blending of individual species or a combination thereof with the antibodies and the excipient of the product.

ABSTRACT WORD COUNT: 125

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9945	513
SPEC A	(English)	9945	2317
Total word count - document A			2830
Total word count - document B			0
Total word count - documents A + B			2830

3/3,AB/15 (Item 7 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01087095
New products comprising inactivated yeasts or moulds provided with active antibodies
Produkten die inaktivierte Hefen oder Schimmel enthalten, die auf ihrer Aussenoberflache aktive Antikorper haben
Produits contenant des levures ou des moisissures inactivees, ayant sur leur surface externe des anticorps actifs
PATENT ASSIGNEE:
Unilever N.V., (200911), Postbus 137, 3130 AC Vlaardingen, NL\(Applicant designated states: , BE; CH; DE; DK; ES; FI; FR; GR; IT; LI; NL; PT; SE; AT)
UNILEVER PLC, (200929), Unilever House Blackfriars P.O. Box 68, London EC4P 4BQ, GB\(Applicant designated states: , GB; IE)
INVENTOR:

Frenken, Leon Gerardus Joseph, Unilever R. Vlaardingen, Olivier van Noortlaan 120, 3133 AT Vlaardingen, (NL)
Harmsen, Michael Marie, ID-DLO, Edelhertweg 15, 8219 PH Lelystad, (NL)
van der Linden, Richard Henricus Jacobus, Universiteit Utrecht, Heidelberglaan 8, 3584 CS Utrecht, (NL)
Verrips, Cornelis Theodorus, Unilever R. Vlaardingen, Olivier van Noortlaan 120, 3133 AT Vlaardingen, (NL)
LEGAL REPRESENTATIVE:
Van Velzen, Maaike Mathilde et al (95421), Unilever N.V. Patent Department Postbus 137, 3130 AC Vlaardingen, (NL)
PATENT (CC, No, Kind, Date): EP 954978 A1 991110 (Basic)
APPLICATION (CC, No, Date): EP 99200439 990216;
PRIORITY (CC, No, Date): EP 98104479 980312
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A23K-001/00

ABSTRACT EP 954978 A1
New products are provided comprising inactivated lower eukaryotic cells, preferably yeasts or moulds, having at the outer surface functionally active antibodies or functionally active fragments thereof. Preferred antibody fragments are the variable domains of Camelidae heavy chain antibodies, which are surprisingly stable against physical and chemical decontamination regimes and do not loose their activity when they are immobilised on the glucan layer of the cell wall which is present in a variety of lower eukaryotes. The new products are preferably in the field of food products, personal care products, and animal feed products.
ABSTRACT WORD COUNT: 94
NOTE:
Figure number on first page: NONE

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9945	452
SPEC A	(English)	9945	7514
Total word count - document A			7966
Total word count - document B			0
Total word count - documents A + B			7966

3/3,AB/16 (Item 8 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01052597
Oral product for the prevention and treatment of infectious gastroenteritides in calves
Oralprodukt zur Pravention und Behandlung von ansteckender Gastroenteritis in Kalbern
Produit oral pour la prevention et le traitement des gastroenterites infectieuses des veaux
PATENT ASSIGNEE:
Medipharm CZ, s.r.o., (2607110), Starovice 215, P O Box 28, 693 01

Hustopece u Brna, (CZ), (Proprietor designated states: all)
INVENTOR:
Mican, Petr, Hradni 43, 693 01 Hustopece u Brna, (CZ)
Stepanek, Jan, Olesinky 14, 592 56 Zvole nad Perstynem, (CZ)
LEGAL REPRESENTATIVE:
McCallum, Graeme David et al (76222), Lloyd Wise, McNeight & Lawrence, Highbank House Exchange Street, Stockport, Cheshire SK3 0ET, (GB)
PATENT (CC, No, Kind, Date): EP 930316 A1 990721 (Basic)
EP 930316 B1 040506
APPLICATION (CC, No, Date): EP 98310267 981215;
PRIORITY (CC, No, Date): CZ 98158 980119
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: C07K-016/02; C07K-016/04; C07K-016/10; C07K-016/12; A61K-039/42; A61K-039/44; A61K-039/44; A61K-39:42; A61K-35:74

ABSTRACT EP 930316 A1
Oral product for the prevention and therapy of infectious gastroenteritis in calves that contents of antibodies to bovine rotavirus, bovine coronavirus and enterotoxigenic strains of Escherichia **coli** prepared from colostrum of immunized cows and/or egg yolks of immunized hens. It contents also a stabilized live culture of lactacidogenic bacteria. Method of production of antibodies to bovine rotavirus, bovine coronavirus and enterotoxigenic strains of Escherichia **coli** by immunization of cows and/or hens with **antigens** of bovine rotavirus, bovine coronavirus and enterotoxigenic strains of Escherichia **coli**, collection of colostrum from the immunized cows and/or egg yolks from the immunized hens and processing of these semi-products into the administration form, for instance by drying.
ABSTRACT WORD COUNT: 112

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	199929	385
CLAIMS B	(English)	200419	366
CLAIMS B	(German)	200419	371
CLAIMS B	(French)	200419	398
SPEC A	(English)	199929	2598
SPEC B	(English)	200419	2881
Total word count - document A			2984
Total word count - document B			4016
Total word count - documents A + B			7000

3/3,AB/17 (Item 9 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01028636
Attaching substances to micro-organisms
Befestigungs-Substanzen an Mikroorganismen
Substances a propriete de fixation sur des microorganismes
PATENT ASSIGNEE:
Rijksuniversiteit te Groningen, (406260), Broerstraat 5, 9712 CP Groningen, (NL), (applicant designated states:

AT;BE;CH;DE;DK;ES;FI;FR;GB;GR;IE;IT;LI;LU;MC;NL;PT;SE)
LEGAL REPRESENTATIVE:
Smulders, Theodorus A.H.J., Ir. et al (21191), Vereenigde Octrooibureaux Nieuwe Parklaan 97, 2587 BN 's-Gravenhage, (NL)
PATENT (CC, No, Kind, Date): EP 916726 A1 990519 (Basic)
APPLICATION (CC, No, Date): EP 97203539 971113;
PRIORITY (CC, No, Date): EP 97203539 971113
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
INTERNATIONAL PATENT CLASS: C12N-015/31; C12N-001/20; C07K-014/315; C07K-014/195; C07K-014/37; C12N-009/36; A61K-038/02; A23L-001/03; G01N-033/68; B01J-020/00;

ABSTRACT EP 916726 A1
The invention relates to surface display of proteins on micro-organisms via the targeting and anchoring of heterologous proteins to the outer surface of cells such as yeast, fungi, mammalian and plant cells, and bacteria. The invention provides a proteinaceous substance comprising a reactive group and at least one attaching peptide which comprises a stretch of amino acids having a sequence corresponding to at least a part of the consensus amino acid sequence listed in figure 10 and comprises a method for attaching a proteinaceous substance to the cell wall of a micro-organism comprising the use of said attaching peptide.
ABSTRACT WORD COUNT: 100

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9920	475
SPEC A	(English)	9920	12958
Total word count - document A			13433
Total word count - document B			0
Total word count - documents A + B			13433

3/3,AB/18 (Item 10 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01021458
Ornithine carbamoyl transferase sequence and uses thereof
Sequenz der Ornithine- Carbamoyl-Transferase und dessen Verwendungen
Sequence de l'ornithine carbamoyl transferase et ses utilisations
PATENT ASSIGNEE:
SMITHKLINE BEECHAM CORPORATION, (201244), One Franklin Plaza P.O. Box 7929, Philadelphia Pennsylvania 19103, (US), (Applicant designated States: all)
INVENTOR:
Zalacain, Magdalena, SmithKline Beecham Pharm., 1250 South Collegeville Road, PO Box 5089, Collegeville, PA 19426-0989, (US)
Brown, James Raymond, SmithKline Beecham Pharm., 1250 South Collegeville Road, PO Box 5089, Collegeville, PA 19426-0989, (US)
LEGAL REPRESENTATIVE:
Mallalieu, Catherine Louise et al (69621), D. Young & Co., 21 New Fetter Lane, London EC4A 1DA, (GB)
PATENT (CC, No, Kind, Date): EP 913476 A2 990506 (Basic)

EP 913476 A3 000301
APPLICATION (CC, No, Date): EP 98203571 981022;
PRIORITY (CC, No, Date): US 961536 971030
DESIGNATED STATES: BE; CH; DE; DK; FR; GB; IT; LI; NL
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: C12N-015/54; C12N-009/10; C12N-005/10; C07K-016/40; C12Q-001/68; A61K-048/00

ABSTRACT EP 913476 A2
The invention provides ornithine carbamoyltransferase polypeptides and DNA (RNA) encoding ornithine carbamoyltransferase polypeptides and methods for producing such polypeptides by recombinant techniques. Also provided are methods for utilizing ornithine carbamoyltransferase polypeptides to screen for antibacterial compounds.
ABSTRACT WORD COUNT: 37

LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	9918	615
SPEC A	(English)	9918	11391
Total word count - document A			12006
Total word count - document B			0
Total word count - documents A + B			12006

3/3,AB/19 (Item 11 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00937994
A LACTIC ACID BACTERIAL REGULATABLE EXPRESSION SYSTEM
MILCHSAUREBAKTERIELLES REGULIERBARES EXPRESSIONSSYSTEM
SYSTEME D'EXPRESSION REGULABLE DE BACTERIES LACTIQUES
PATENT ASSIGNEE:
Bioteknologisk Institut, (1788812), Kogle Alle 2, 2970 Hoersholm, (DK), (Proprietor designated states: all)
INVENTOR:
MADSEN, Soeren, Michael, 1st floor, Baldersgade 11, DK-2200 Copenhagen N, (DK)
VRANG, Astrid, Langs Hegnet 76, DK-2800 Lyngby, (DK)
ARNAU, Jose, Melvillevej 9, DK-2900 Hellerup, (DK)
RAVN, Peter, Naerum Hovedgade 9A, DK-2850 Naerum, (DK)
GROENVALD JOHNSEN, Mads, 3rd floor, Sveasvej 5, DK-1917 Frederiksberg C, (DK)
ISRAELSEN, Hans, Proevestensvej 1A, DK-3450 Alleroed, (DK)
LEGAL REPRESENTATIVE:
Plougmann, Vingtoft & Partners A/S (101171), Sankt Annae Plads 11, P.O. Box 3007, 1021 Copenhagen K, (DK)
PATENT (CC, No, Kind, Date): EP 925364 A1 990630 (Basic)
EP 925364 B1 021023
WO 98010079 980312
APPLICATION (CC, No, Date): EP 97936612 970822; WO 97DK341 970822
PRIORITY (CC, No, Date): US 711434 960906
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; [illegible]; NL; PT; SE

INTERNATIONAL PATENT CLASS: C12N-015/74; C12N-001/21; A23C-009/12;
A23L-001/03; C07K-014/35; C12N-015/31; C12N-015/62
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200243	1661
CLAIMS B	(German)	200243	1497
CLAIMS B	(French)	200243	1768
SPEC B	(English)	200243	18946
Total word count - document A			0
Total word count - document B			23872
Total word count - documents A + B			23872

3/3,AB/20 (Item 12 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00864007
DETECTION OF BACTERIUM BELONGING TO THE GENUS PECTINATUS
NACHWEIS EINER BAKTERIE DER PECTINATUS GATTUNG
PROCEDE DE DETECTION D'UNE BACTERIE APPARTENANT AU GENRE PECTINATUS
PATENT ASSIGNEE:
ASAHI BREWERIES, LTD., (947071), 7-1, Kyobashi 3-chome Chuoh-ku, Tokyo 104, (JP), (Proprietor designated states: all)
INVENTOR:
SAKAMOTO, Kanta, Asahi Breweries, Ltd. Sakerui Kenkyusho-nai, 2-13-1, Oumori Kita Outa-ku Tokyo 143, (JP)
LEGAL REPRESENTATIVE:
Sheard, Andrew Gregory et al (50962), Kilburn & Strode 20 Red Lion Street , London WC1R 4PJ, (GB)
PATENT (CC, No, Kind, Date): EP 806483 A1 971112 (Basic)
EP 806483 B1 040128
WO 1997020071 970605
APPLICATION (CC, No, Date): EP 96939308 961127; WO 96JP3464 961127
PRIORITY (CC, No, Date): JP 95331172 951128; JP 95331173 951128
DESIGNATED STATES: DE; FI; GB; NL
INTERNATIONAL PATENT CLASS: C12Q-001/68; C12N-015/11; C07H-021/04
ABSTRACT EP 806483 A1

A method of detecting specific species of the genus Pectinatus detrimental to beer by using an oligonucleotide which targets a nucleotide sequence encoding the 16S ribosomal RNA gene of a bacterium belonging to the genus Pectinatus and is complementary to this nucleotide sequence so as to selectively detect the specific bacterium in a sample, characterized in that the oligonucleotide has a group of specified sequences or a group of complementary sequences corresponding thereto.

ABSTRACT WORD COUNT: 74

LANGUAGE (Publication,Procedural,Application): English; English; Japanese
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	199711W1	394
CLAIMS B	(English)	200405	178
CLAIMS B	(German)	200405	174

CLAIMS B	(French)	200405	179
SPEC A	(English)	199711W1	3368
SPEC B	(English)	200405	3767
Total word count - document A			3763
Total word count - document B			4298
Total word count - documents A + B			8061

3/3,AB/21 (Item 13 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00806722
USE OF EPITHELIAL ADHESIVE LACTOBACILLI
VERWENDUNG VON EPITHEL-ADHARENTE LACTOBAZILLEN
UTILISATION DE LACTOBACILLI ADHERANT AUX CELLULES EPITHELIALES
PATENT ASSIGNEE:
PROBI AB, (1587431), Solvegatan 41, 223 70 Lund, (SE), (Proprietor designated states: all)
INVENTOR:
ADLERBERTH, Ingegerd, O. Skansgatan 3B, S-413 02 Goteborg, (SE)
AHRNE, Siv, Domarevagen 19, S-237 31 Bjarred, (SE)
JEPPSSON, Bengt, Mataregrand 8, S-222 47 Lund, (SE)
JOHANSSON, Marie-Louise, Flygelvagen 14, S-226 46 Lund, (SE)
MOLIN, Goran, Examensvagen 2, S-224 67 Lund, (SE)
WOLD, Agnes, Antilopgatan 8, S-431 38 Molndal, (SE)
LEGAL REPRESENTATIVE:
Andersson, Bjorn et al (88803), Awapatent AB, P.O. Box 5117, 200 71 Malmo, (SE)
PATENT (CC, No, Kind, Date): EP 817640 A1 980114 (Basic)
EP 817640 B1 030521
WO 96029083 960926
APPLICATION (CC, No, Date): EP 96908428 960325; WO 96SE372 960325
PRIORITY (CC, No, Date): SE 951056 950323
DESIGNATED STATES: AT; BE; CH; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: LT; LV
INTERNATIONAL PATENT CLASS: A61K-035/74; A61P-013/02; A61P-031/04
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS B	(English)	200321	84
CLAIMS B	(German)	200321	80
CLAIMS B	(French)	200321	94
SPEC B	(English)	200321	5864
Total word count - document A			0
Total word count - document B			6122
Total word count - documents A + B			6122

3/3,AB/22 (Item 14 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00423980
Immunostimulant agent
Immunostimulierendes Mittel
Agent immunostimulant
PATENT ASSIGNEE:
SOCIETE DES PRODUITS NESTLE S.A., (229220), Case postale 353, 1800 Vevey, (CH), (Proprietor designated states: all)
INVENTOR:
Link, Harriet, Boulevard St.-Martin 16, CH-1800 Vevey, (CH)
Pahud, Jean-Jacques, Baumaroche 2, CH-1801 Mont-Pelerin, (CH)
PATENT (CC, No, Kind, Date): EP 432490 A2 910619 (Basic)
EP 432490 A3 910821
EP 432490 B1 950830
EP 432490 B2 010516
APPLICATION (CC, No, Date): EP 90121752 901114;
PRIORITY (CC, No, Date): CH 894484 891213
DESIGNATED STATES: AT; BE; DE; DK; ES; FR; GB; GR; IT; LU; NL; SE
INTERNATIONAL PATENT CLASS: A61K-039/07; A23C-009/12

ABSTRACT EP 432490 A2 (Translated)
Immunostimulant agent comprising N-acetyl-muramyl-peptides derived from peptidoglycans of the cell wall of lysozyme-sensitive lactic bacteria.
TRANSLATED ABSTRACT WORD COUNT: 17

ABSTRACT EP 432490 A2
Agent immunostimulant comprenant des N-acetyl-muramyl-peptides derives de peptidoglycanes de la paroi cellulaire de bacteries lactiques sensibles au lysozyme.
ABSTRACT WORD COUNT: 20

LANGUAGE (Publication,Procedural,Application): French; French; French
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(French)	EPABF1	272
CLAIMS B	(English)	200120	269
CLAIMS B	(German)	200120	263
CLAIMS B	(French)	200120	274
SPEC A	(French)	EPABF1	2755
SPEC B	(French)	200120	3003
Total word count - document A			3027
Total word count - document B			3809
Total word count - documents A + B			6836

3/3,AB/23 (Item 15 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

00223100
Anti-human interleukin 1 antibody, method for the production thereof and use of the same.
Antihumaninterleukin-1-Antikorper, Verfahren zu seiner Herstellung und seine Anwendung.
Anticorps anti-interleukine-1 humaine, methode pour sa production et son utilisation.
PATENT ASSIGNEE:

Dainippon Pharmaceutical Co., Ltd., (218460), 25, Doshomachi 3-chome Higashi-ku, Osaka-shi, Osaka 541, (JP), (applicant designated states: BE;CH;DE;ES;FR;GB;IT;LI;NL;SE)
INVENTOR:
Yamada, Masaaki, 13, Murasakino-Nishiren-Daino-Cho Kita-ku, Kyoto-shi Kyoto-fu, (JP)
Kawata, Shigeo, 15-12, Wakabadai 2-chome Kita-ku, Kobe-shi Hyogo-ken, (JP)
Sunahara, Noriyuki, 86-2, Kawashimaarisugawa-cho Nishikyo-ku, Kyoto-shi Kyoto-fu, (JP)
Furuta, Ryuji, 24-8, Fujimidai, Otsu-shi Shiga-ken, (JP)
Yamayoshi, Michiko, 8-14, Nishi-Midorigaoka 3-chome, Toyonaka-shi Osaka-fu, (JP)
LEGAL REPRESENTATIVE:
Harrison, David Christopher et al , MEWBURN ELLIS & CO 2/3 Cursitor Street, London EC4A 1BQ, (GB)
PATENT (CC, No, Kind, Date): EP 220063 A2 870429 (Basic)
EP 220063 A3 881005
APPLICATION (CC, No, Date): EP 86308027 861016;
PRIORITY (CC, No, Date): JP 85233004 851017
DESIGNATED STATES: BE; CH; DE; ES; FR; GB; IT; LI; NL; SE
INTERNATIONAL PATENT CLASS: C12P-021/00; C07K-003/20; G01N-033/577;

ABSTRACT EP 220063 A2
An antibody, especially a monoclonal antibody, against a human interleukin 1 polypeptide having a particular amino acid sequence may be produced by forming a hybridoma cell between an antibody-producing cell of an animal immunized with the polypeptide and a myeloma cell, cloning the hybridoma cell and producing the anti-polypeptide antibody with a selected clone capable of such production.
The antibody can be used for the purification of the polypeptide and for the quantitative determination of human interleukin 1 by assays such as EIA and RIA.
ABSTRACT WORD COUNT: 89
LANGUAGE (Publication,Procedural,Application): English; English; English
FULLTEXT AVAILABILITY:

Available Text	Language	Update	Word Count
CLAIMS A	(English)	EPABF1	344
SPEC A	(English)	EPABF1	5234
Total word count - document A			5578
Total word count - document B			0
Total word count - documents A + B			5578

3/3,AB/24 (Item 1 from file: 357)
DIALOG(R)File 357:DERWENT BIOTECH RES.

0336585 DBR Accession No.: 2004-08877 PATENT
Inducing an immune response in an animal comprises providing an immunogenic composition comprising a microflora organism having an expression vector comprising a heterologous nucleic acid that encodes for an **antigen** - immunogenic composition and vector expression in host cell for use in disease therapy
AUTHOR: CHEN W; FU X; NOURAINI S; ZHANG Z
PATENT ASSIGNEE: CHEN W; FU X; NOURAINI S; ZHANG Z 2004

PATENT NUMBER: US 20040009937 PATENT DATE: 20040115 WPI ACCESSION NO.: 2004-098616 (200410)
PRIORITY APPLIC. NO.: US 353137 APPLIC. DATE: 20030127
NATIONAL APPLIC. NO.: US 353137 APPLIC. DATE: 20030127
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - Inducing an immune response in an animal comprises providing an immunogenic composition formulated for intranasal administration to the animal where immunogenic composition comprises a microflora organism having an expression vector comprising a heterologous nucleic acid that encodes for an **antigen**. DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for an immunogenic composition comprising an intranasal formulation of a microflora organism having an expression vector that comprises a heterologous nucleic acid that encodes for an **antigen** . BIOTECHNOLOGY - Preferred Method: In inducing an immune response, the microflora organism is yeast or bacteria. The **antigen** is selected from tumors, bacteria, viruses, parasites, and fungi. The **viruses** are selected from **influenza**, hepatitis, HIV, and rotavirus. The yeast is selected from Saccharomyces cerevisiae, S. exiquus, S. telluris, S. dairensis, S. servazzii, S. unisporus, and S. kluyveri. The bacteria is selected from the group consisting of Bifidobacterium sp, Streptococcus thermophilus, Enterococcus faecalis, Enterococcus durans, Lactococcus lactis, Lactobacillus lactis, Lactobacillus acidophilus, Lactobacillus bulgaricus, Lactobacillus thermophilus, Lactobacillus casei and **Lactobacillus plantarum** . The intranasal formulation is selected from powder, a freeze-dried powder a liquid preparation, a semi-solid, yogurt milk and cheese. The method alternatively comprises providing an intranasal formulation of transformed yeast where yeast comprise a heterologous nucleic acid encoding for an **antigen** that is expressed on the surface of the yeast. The **antigen** is derived from a virus. The method preferably comprises providing an intranasal formulation of transformed Saccharomyces cerevisiae comprising a heterologous nucleic acid encoding for an immunoprotective epitope from influenza A. The immunoprotective epitope is influenza HA or NA. Preferred Composition: The intranasal formulation is selected from aerosols, drops, snuffs, suppositories and creams. The bacteria is fused with an E. **coli** is selected from HB101, C600, DH1, DHaS and P10. The E. **coli** comprises a plasmid. The plasmid comprises a heterologous nucleic acid operably linked to a promoter capable of driving expression of said heterologous nucleic acid in a host organism. The heterologous nucleic acid codes for an **antigen**. The **antigen** is expressed on the bacteria's cell surface. The **antigen** is secreted. The **antigen** is selected from Mycobacterium leprae **antigens**, Mycobacterium tuberculosis **antigens**, Rickettsia **antigens**, Chlamydia **antigens**, Coxiella **antigens**, malaria sporozoite and merozoite protein **antigens**, the circumsporozoite protein **antigen** from Plasmodium berghei sporozoites, diphtheria toxoids, tetanus toxoids, Clostridium **antigens**, Leishmania **antigens**, Salmonella **antigens**, E. **coli antigens**, Listeria **antigens**, Borrelia **antigens**, the OspA and OspB **antigens** of Borrelia burgdorferi, Franciscella **antigens**, Yersinia **antigens**, Mycobacterium africanum **antigens**, Mycobacterium intracellular **antigens**, Mycobacterium avium **antigens**, Treponema **antigens**, Schistosome **antigens**, Filaria **antigens**, Pertussis **antigens**, Staphylococcus **antigens**, Hemophilus

antigens, Streptococcus **antigens** , the M protein of S. pyogenes, Pneumococcus **antigens**, Shigella **antigens** , Neisseria **antigens**, Anthrax toxin, Clostridium, Staphylococcus, Helicobacter, Pseudomona, Yersinia, rabies virus, Salmonella and Pneumonia. The **antigen** is selected from the mumps virus **antigens**, hepatitis virus a.b.c.d.e. HBV **antigens**, Herpes virus **antigens**, parainfluenza virus **antigens**, rabies **antigens**, polio virus **antigens**, Rift Valley Fever virus **antigens**, dengue virus **antigens**, measles virus **antigens**, rotavirus **antigens**, Human Immunodeficiency Virus (HIV) **antigens**, the gag, pol, and env protein **antigens**, gp 120 and gp 160 of the HIV env, respiratory syncytial virus (RSV) **antigens**, snake venom **antigens**, human tumor **antigens**, Vibrio cholera **antigens** , HCV, HAV, HPV, TB, Herpes, rubella, influenza, poliomyelitis, rotavirus, surface glycoprotein of malaria parasite, Epstein barr virus, poxvirus, rabies virus, CEA and cancer **antigens**. ACTIVITY - Immunosuppressive; Antibacterial; Virucide. No biological data given. MECHANISM OF ACTION - Vaccine. USE - The methods are compositions are useful for inducing an immune response against viral and bacterial infections. ADMINISTRATION - Administration is intranasal (claimed). No dosage is given. EXAMPLE - Experimental protocols are described but no results are given. (30 pages)

3/3,AB/25 (Item 2 from file: 357)
DIALOG(R)File 357:DERWENT BIOTECH RES.

0322340 DBR Accession Number: 2003-23480 PATENT
Immunogenic composition useful for inducing immune response against tumor, comprising oral formulation of microflora organism having expression vector having heterologous nucleic acid that encodes for **antigen** - involving vector-mediated gene transfer and expression in host cell for use in cancer and infection therapy
AUTHOR: CHEN W; FU X; NOURAINI S; ZHANG Z
PATENT ASSIGNEE: SYMBIGENE INC 2003
PATENT NUMBER: WO 200363785 PATENT DATE: 20030807 WPI ACCESSION NO.: 2003-636770 (200360)
PRIORITY APPLIC. NO.: US 401465 APPLIC. DATE: 20020805
NATIONAL APPLIC. NO.: WO 2003US2468 APPLIC. DATE: 20030127
LANGUAGE: English
ABSTRACT: DERWENT ABSTRACT: NOVELTY - An immunogenic composition (C1) comprising an oral formulation of a microflora organism having an expression vector that comprises a heterologous nucleic acid encoding an **antigen** .BIOTECHNOLOGY - Preferred Composition: In (C1), the microflora organism is a yeast or bacteria. The yeast is chosen from Saccharomyces cerevisiae, S.exiquus, S.telluris, S.dairensis, S.servazzii, S.unisporus and S.kluyveri. The bacteria is chosen from Bifidobacterium, Streptococcus thermophilus, Enterococcus faecalis, E.durans, Lactococcus lactis, Lactobacillus lactis, L.acidophilus, L.bulgaricus, L.thermophilus, L.casei and **L.plantarum**. The oral formulation is chosen from powder, a freeze dried powder, a liquid preparation, a semi-solid, yogurt milk and cheese. (C1) preferably comprises an oral formulation of transformed yeast (S.cerevisiae), where the yeast comprise a heterologous nucleic acid encoding for a **antigen** (immunoprotective epitope from influenza A), and the

antigen is expressed on the surface of yeast. The immunoprotective epitope is influenza hemagglutinin (HA) or neuraminidase (NA). ACTIVITY - Cytostatic; Antibacterial; Virucide; Antiparasitic; Fungicide; Anti-HIV. MECHANISM OF ACTION - Inducer of immune response (claimed). The immune response inducing activity of (C1) was evaluated by using female Balb/c mice. Six weeks old female Balb/c mice were inoculated by oral, intranasal or subcutaneous routes with yeast displaying VP7, hemagglutinin (HA) or neuraminidase (NA) on the cell surface. Booster inoculations were performed every two weeks. Mice were inoculated with either yeast expressing surface-displayed **antigen** or yeast containing empty vector. Blood samples were collected before the first vaccination (oral: 0.1 ml (5x108)/mice) and every two weeks thereafter. Mice were sacrificed after 8-weeks. Antibody response were measured by taking blood samples (0.1 ml) from the eye bowl. Serum were separated by centrifugation, and stored at -20 degrees C. The lung and intestine were separated from the sacrificed animal and washed with phosphate buffered saline (PBS). The tissue washings were centrifuged and the supernatants were stored at -20 degrees C. The viral **antigens** VP7, HA or NA were coated on 96 well plates. After blocking of non-specific binding sites, samples of sera, lung or intestine washings were diluted with PBS and added to each well. Horseradish peroxidase-labeled secondary antibodies (anti-IgG or anti-IgA) were used to detect antibody-**antigen** complexes. When compared to the plasmid controls, each immunogenic composition successfully elicited an immune response in the test animal. USE - (C1) is useful for inducing an immune response in an animal which involves providing (C1) formulated for oral administration to the animal. The **antigen** is chosen from tumors, bacteria, **viruses** (e.g., **influenza**, hepatitis, HIV, and rotavirus), parasites, and fungi. (C1) is useful for inducing an immune response in an animal which involves providing an oral formulation of transformed yeast (S.cerevisiae), where yeast comprise a heterologous nucleic acid encoding for an **antigen** (immunoprotective epitope from influenza A), and the **antigen** is expressed on surface of the yeast (claimed). ADMINISTRATION - (C1) is administered by oral routes (claimed); rectal or vaginal routes;and intratracheobronchial routes. No dosage details are given. EXAMPLE - Lactobacillus acidophilus protoplasts were formed by growing L.acidophilus cells in MRS broth (undefined) at 37 degrees C for 3 hours to overnight. The cells were then centrifuged at 2000 x g for 30 minutes and the resulting cell pellet washed and resuspended in hypertonic solution (0.01 M Tris hydrochloride (pH 7.5), 0.3-0.5 M mannitol) that contained lysozyme (20 microg/ml) and incubated at room temperature for 5-15 minutes. The resulting protoplasts were gently overlaid on plates with the appropriate regeneration media or formulated by mixing with suitable carriers such as yogurts or hypertonic solution having sucrose and appropriate buffers. An expression cassette comprising an autolyzing gene such as AcmA, holin or lysin was operably linked to a lactose promoter such as the bacterial Plac promoter or a pH dependent promoter. With respect to the Plac promoter for example, this was achieved by cloning the autolyzing gene in pBluescript from stratagene cloning system. Clones to be used were chosen to contain certain biochemical enzymes involved in the pathway for metabolizing certain nutrients or amino acids such as tryptophan and tyrosine, and the insertion of pBluescript disrupts the particular enzyme in the particular metabolic pathway. The resulting modified genomic DNA clone

were transformed back into Lactobacillus using transformation protocols. When the modified genomic DNA clone was in the cell, it was homologously recombined with the endogenous chromosomal DNA and resulted in integration of autolyzing gene into the Lactobacillus genome. Selection of mutants was by antibiotic resistance conferred by pBlueScript plasmid or with the loss of the cell ability to grow with the nutrients whose metabolic pathway was been disrupted. The culture of these protoplasts having targeting compound were incubated with M-cell in vitro. (82 pages)

Set	Items	Description
S4	3409	AU=(SHAW, D? OR SHAW D?)
S5	95	AU=(LEER R? OR LEER, R?)
S6	28	AU=(POUWELS H? OR POUWELS, H?)
S7	0	S4 AND S5 AND S6
S8	7	S4 AND (S5 OR S6)
S9	0	S5 AND S6
S10	3525	S4 OR S5 OR S6
S11	8	S10 AND S1
S12	6	(S8 OR S11) NOT S2
S13	4	RD (unique items)

>>>No matching display code(s) found in file(s): 65, 113

13/3,AB/1 (Item 1 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

11942960 References: 23
TITLE: Engineering the microflora to vaccinate the mucosa: serum immunoglobulin G responses and activated draining cervical lymph nodes following mucosal application of tetanus toxin fragment C-expressing lactobacilli
AUTHOR(S): **Shaw DM (REPRINT)**; Gaerthe B; **Leer RJ**; Van der Stap JGMM; Smittenaar C; Den Bak-Glashouwer MJH; Thole JER; Tielen FJ; Pouwels PH; Havenith CEG
CORPORATE SOURCE: TNO Prevent & Hlth, Special Program Infect Dis, Zernikedreef 9,POB 2215/NL-2315 CE Leiden//Netherlands/ (REPRINT); TNO Prevent & Hlth, Special Program Infect Dis, /NL-2315 CE Leiden//Netherlands/; TNO Voeding, Dept Mol Genet & Gene Technol, /Zeist//Netherlands/
PUBLICATION TYPE: JOURNAL
PUBLICATION: IMMUNOLOGY, 2000, V100, N4 (AUG), P510-518
GENUINE ARTICLE#: 347PR
PUBLISHER: BLACKWELL SCIENCE LTD, P O BOX 88, OSNEY MEAD, OXFORD OX2 0NE, OXON, ENGLAND
ISSN: 0019-2805
LANGUAGE: English DOCUMENT TYPE: ARTICLE
ABSTRACT: The delivery of **antigens** to mucosal-associated lymphoid tissues in paediatric and immunocompromised populations by safe, non-invasive vectors, such as commensal lactobacilli, represents a crucial improvement to prevailing vaccination options. In this report, we describe the oral and nasal immunization of mice with vaccines constructed through an original system for heterologous gene expression in Lactobacillus in which the 50 000-molecular weight (MW) fragment C of tetanus toxin (TTFC) is expressed either as an intracellular or a surface-exposed protein. Our data indicate that **L. plantarum** is more effective in this

respect than L. casei and that, under the experimental conditions investigated, delivery of TTFC expressed as an intracellular **antigen** is more effective than cell-surface expression. Immunization of mice with live recombinant lactobacilli induced significant levels of circulating TTFC-specific immunoglobulin G (IgG) following nasal or oral delivery of vaccine strains. In addition, following nasal delivery, secretory immunoglobulin A (sIgA) was induced in bronchoalveolar lavage fluids, as were **antigen**-specific antibody-secreting cells and **antigen** -specific T-cell activation in draining lymph nodes, substantiating their potential for safe mucosal delivery of paediatric vaccines.

13/3,AB/2 (Item 2 from file: 440)
DIALOG(R)File 440:Current Contents Search(R)

10541785 References: 31
TITLE: Instruments for oral disease-intervention strategies: recombinant Lactobacillus casei expressing tetanus toxin fragment C for vaccination or myelin proteins for oral tolerance induction in multiple sclerosis
AUTHOR(S): Maassen CBM; Laman JD (REPRINT); den Bak-Glashouwer MJH; Tielen FJ; van Holten-Neelen JCPA; Hoogteijling L; Antonissen C; **Leer RJ**; Pouwels PH; Boersma WJA; **Shaw DM**
AUTHOR(S) E-MAIL: jd.laman@pg.tno.nl
CORPORATE SOURCE: TNO Prevent & Hlth PG, Div Immunol & Infect Dis, POB 2215/NL-2301 CE Leiden//Netherlands/ (REPRINT); TNO Prevent & Hlth PG, Div Immunol & Infect Dis, /NL-2301 CE Leiden//Netherlands/; Erasmus Univ, Dept Immunol, /NL-3000 DR Rotterdam//Netherlands/; TNO, Dept Mol Genet & Gene Technol, /NL-3700 AJ Zeist//Netherlands/; DLO, Dept Immunol, /NL-8200 AB Lelystad//Netherlands/
PUBLICATION TYPE: JOURNAL
PUBLICATION: VACCINE, 1999, V17, N17 (APR 23), P2117-2128
GENUINE ARTICLE#: 192AK
PUBLISHER: ELSEVIER SCI LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, OXON, ENGLAND
ISSN: 0264-410X
LANGUAGE: English DOCUMENT TYPE: ARTICLE

ABSTRACT: Lactobacillus strains possess properties that make them attractive candidates as vehicles for oral administration of therapeutics, In this report we describe the construction and analysis of recombinant Lactobacillus casei applicable in oral vaccination against an infectious disease (tetanus) and in oral tolerance induction for intervention in an autoimmune disease, multiple sclerosis.

Recombinant L. casei which express surface-anchored tetanus toxin fragment C (TTFC) were generated. Quantitative analysis by Bow cytometry demonstrated a high level of cell wall-bound expression of TTTFC and immunogenicity was demonstrated by parenteral immunization with whole cell extracts of the recombinants,

A series of expression vectors was constructed to secrete human myelin basic protein (hMBP) or hMBP as a fusion protein with beta-glucuronidase from Escherichia coli. These heterologous products produced by L. casei were detected in the growth medium and parenteral immunization with this medium evoked antibodies against hMBP, confirming that secretion indeed had

occurred.

Based on the different localization of the heterologous proteins. lactobacilli expressing surface-anchored TTFC are ideally suited for the induction of antibody responses, whereas lactobacilli that secrete myelin proteins can be used for the induction of peripheral T-cell tolerance. In conclusion, the specific technology described here allows the construction of a wide array of safe live recombinant lactobacilli which may prove to be useful in oral intervention strategies for the prevention of infectious diseases or treatment of autoimmune diseases.

13/3,AB/3 (Item 1 from file: 348)
DIALOG(R)File 348:EUROPEAN PATENTS

01282155
ORAL RECOMBINANT LACTOBACILLI VACCINES
ORALE REKOMBINANTE LACTOBACILLI IMPFSTOFF
VACCINS ORAUX A BASE DE LACTOBACILLES RECOMBINEES
PATENT ASSIGNEE:
NEDERLANDSE ORGANISATIE VOOR TOEGEPAST-NATUURWETENSCHAPPELIJK ONDERZOEK TNO, (285526), Schoemakerstraat 97, P.O. Box 60680, 2628 VK Delft, (NL), (Applicant designated States: all)
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PATENT (CC, No, Kind, Date): EP 1212083 A1 020612 (Basic)
WO 200121200 010329
APPLICATION (CC, No, Date): EP 2000962689 000918; WO 2000GB3575 000918
PRIORITY (CC, No, Date): EP 99203056 990917
DESIGNATED STATES: AT; BE; CH; CY; DE; DK; ES; FI; FR; GB; GR; IE; IT; LI; LU; MC; NL; PT; SE
EXTENDED DESIGNATED STATES: AL; LT; LV; MK; RO; SI
INTERNATIONAL PATENT CLASS: A61K-039/00; C12N-015/74
NOTE:
No A-document published by EPO
LANGUAGE (Publication,Procedural,Application): English; English; English

13/3,AB/4 (Item 1 from file: 357)
DIALOG(R)File 357:DERWENT BIOTECH RES.

0268568 DBR Accession No.: 2001-08874 PATENT
Oral vaccine based on recombinant **Lactobacillus plantarum**, useful for protecting against microbial pathogens and allergens, expresses heterologous **antigen** - plasmid pLP503-TTFC-mediated TTFC tetanus **antigen** gene transfer, expression in host cell and immunization in mouse for recombinant vaccine and bacterium, virus,

fungus or protozoon infection therapy
AUTHOR: **Shaw D M; Leer R J;** Pouwels P
CORPORATE SOURCE: Delft, The Netherlands.
PATENT ASSIGNEE: TNO 2001
PATENT NUMBER: EP 1084709 PATENT DATE: 20010321 WPI ACCESSION NO.: 2001-246878 (2026)
PRIORITY APPLIC. NO.: EP 99203056 APPLIC. DATE: 19990917
NATIONAL APPLIC. NO.: EP 99203056 APPLIC. DATE: 19990917
LANGUAGE: English
ABSTRACT: An oral vaccine (A) containing a recombinant lactic acid bacterium that expresses a heterologous **antigen** (Ag) in vivo, intracellularly and/or at the cell surface, as the immunogenicity-eliciting component (the bacterium used is **Lactobacillus plantarum**), is claimed. Also claimed are: a recombinant **L. plantarum** (strain 256), for use in the vaccines; and an expression vector for intracellular expression and exposure of Ag by **L. plantarum** under the conditions that exist in the gastrointestinal tract. **L. plantarum** containing the plasmid pLP503-TTFC (expressing intracellularly the TTFC tetanus **antigen**) was administered orally (5 x 10(9) cells) to mice. Following two booster doses, the TTFC-specific antibody titer increased to 10(3) by day 77. (A) are used to protect against a wide range of bacteria, viruses, fungi and protozoa, especially those that colonize the mucosa or gastrointestinal tract and also against allergens. (19pp)
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